

2001

Mary Hale Please!

Access DB#

## SEARCH REQUEST FORM

## Scientific and Technical Information Center

Requester's Full Name: K. Weddington Examiner #: 68082 Date: 3-31-03Art Unit: 1614 Phone Number 308-4650 Serial Number: 091889820Mail Box and Bldg/Room Location: CM-1-2A17 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention:

Inventors (please provide full names): David Thomas ~~and~~ Davies; Caroline Joan Henry  
Neil Pearson

Earliest Priority Filing Date:

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

A method of treatment of bacterial infections with  
formula (I)

Mary Hale - Supervisor, Info. Branch  
STIC - Biotech/Chem. Library  
CM-1-Room E01  
703-308-4258

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## STAFF USE ONLY

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Searcher:

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Searcher Location:

Date Searcher Picked Up:

Date Completed: 4/3

Searcher Prep &amp; Review Time:

Clerical Prep Time:

Online Time:

## Type of Search

## Vendors and cost where applicable

NA Sequence (#)

STN

AA Sequence (#)

Dialog

Structure (#)

Questel/Orbit

Bibliographic

Dr. Link

Litigation

Lexis/Nexis

Fulltext

Sequence Systems

Patent Family

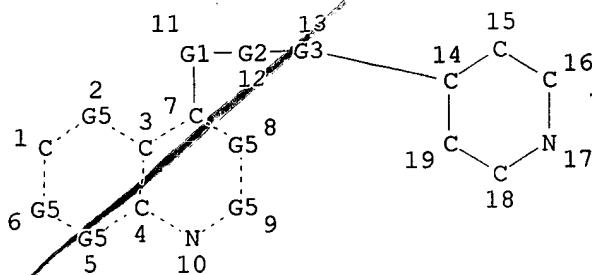
WWW/Internet

Other

Other (specify)

Waddington  
889820

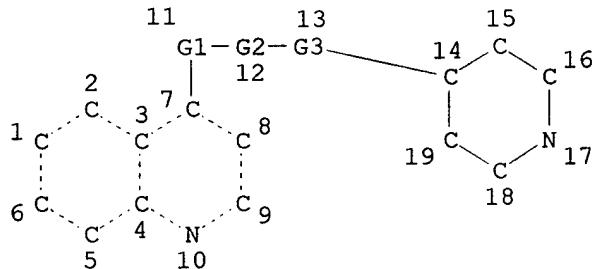
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REP G3=(0-2) CH2  
VAR G5=C/N  
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
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NUMBER OF NODES IS 19

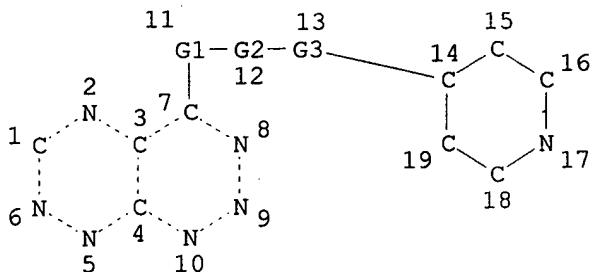
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L3 STR



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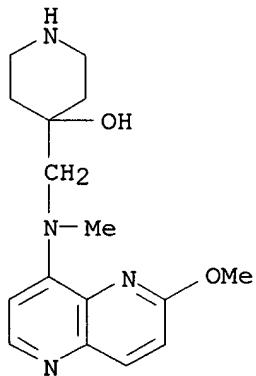
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L4 STR



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 DEFAULT ECLEVEL IS LIMITED  
 GRAPH ATTRIBUTES:  
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 NUMBER OF NODES IS 19  
 STEREO ATTRIBUTES: NONE  
 L7 42 SEA FILE=REGISTRY SSS FUL L1 NOT (L3 OR L4)  
 100.0% PROCESSED 33013 ITERATIONS  
 SEARCH TIME: 00.00.01

42 ANSWERS

L7 ANSWER 1 OF 42 REGISTRY COPYRIGHT 2003 ACS  
 RN 495416-19-8 REGISTRY  
 CN 4-Piperidinol, 4-[(6-methoxy-1,5-naphthyridin-4-yl)methylamino]methyl]-  
 (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C16 H22 N4 O2  
 SR CA  
 LC STN Files: CA, CAPLUS



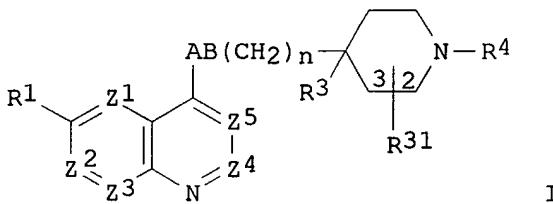
Searched by: Mary Hale 308-4258 CM-1 1E01

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1 REFERENCES IN FILE CA (1962 TO DATE)  
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REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

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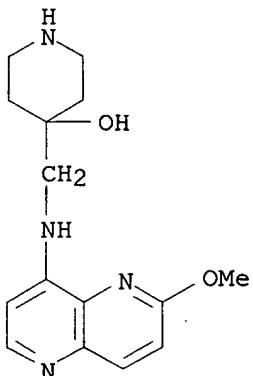


I

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.mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMCl, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

L7 ANSWER 2 OF 42 REGISTRY COPYRIGHT 2003 ACS  
RN 495416-16-5 REGISTRY  
CN 4-Piperidinol, 4-[(6-methoxy-1,5-naphthyridin-4-yl)amino]methyl]- (9CI)  
(CA INDEX NAME)  
OTHER NAMES:  
CN 4-[(6-Methoxy-[1,5]naphthyridin-4-ylamino)methyl]piperidin-4-ol  
FS 3D CONCORD  
MF C15 H20 N4 O2  
SR CA  
LC STN Files: CA, CAPLUS

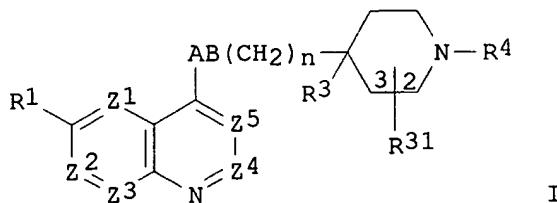


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L7 ANSWER 3 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 495416-15-4 REGISTRY

CN 1-Piperidinecarboxylic acid, 4-hydroxy-4-[[[(6-methoxy-1,5-naphthyridin-4-yl)amino]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4-Hydroxy-4-[(6-methoxy-[1,5]naphthyridin-4-ylamino)methyl]piperidine-1-carboxylic acid tert-butyl ester

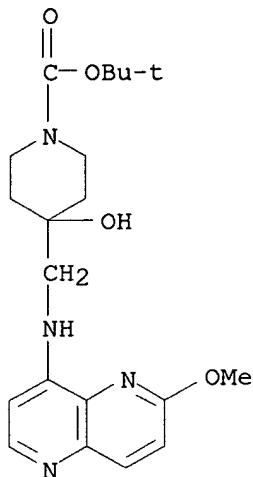
FS 3D CONCORD

MF C20 H28 N4

SB CA

SR ST  
LC ST'

EC SIN FILES. CA, CAT EBUS

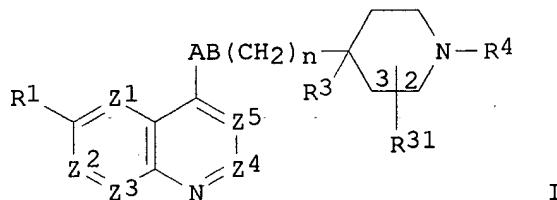


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2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF<sub>3</sub>, C1-6 alkoxy carbonyl, C1-6 alkyl carbonyl, C2-6 alkenyloxy carbonyl, C2-6 alkenyl carbonyl, (un)substituted OH or NH<sub>2</sub>, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH<sub>2</sub>R51, U-V-R52 (wherein R51 = C4-8 alkyl, hydroxy-C4-8 alkyl, C1-4 alkoxy-C4-8 alkyl, etc.; U = CO, SO<sub>2</sub>, CH<sub>2</sub> and V = (un)substituted CH<sub>2</sub>; or U = CH<sub>2</sub> and V = CO, (un)substituted C(:NOH), SO<sub>2</sub>; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH<sub>2</sub>, CH<sub>2</sub>CO, OCH<sub>2</sub>, CH<sub>2</sub>O, NHCH<sub>2</sub>, CH<sub>2</sub>NH, NHSO<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>] and pharmaceutically acceptable derivs. thereof are prep'd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K<sub>2</sub>CO<sub>3</sub> in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of .1toreq.4 .mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMC1, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

L7 ANSWER 4 OF 42 REGISTRY COPYRIGHT 2003 ACS

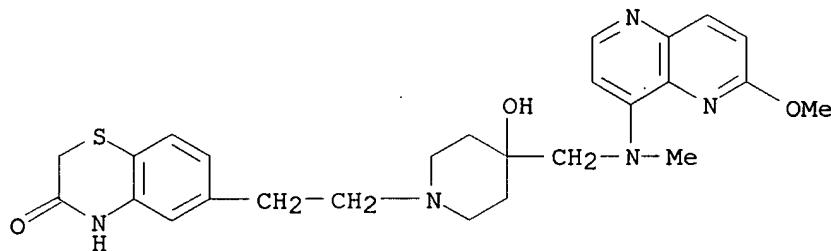
RN 495416-14-3 REGISTRY

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MF C26 H31 N5 O3 S . 2 Cl H

SR CA

LC STN Files: CA, CAPLUS



●2 HCl

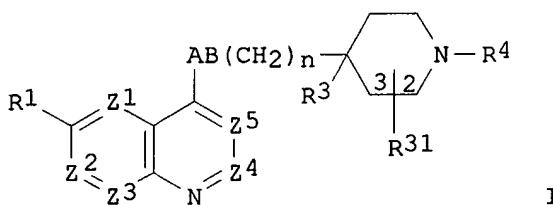
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GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US,  
UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE,  
BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT,  
LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN:  
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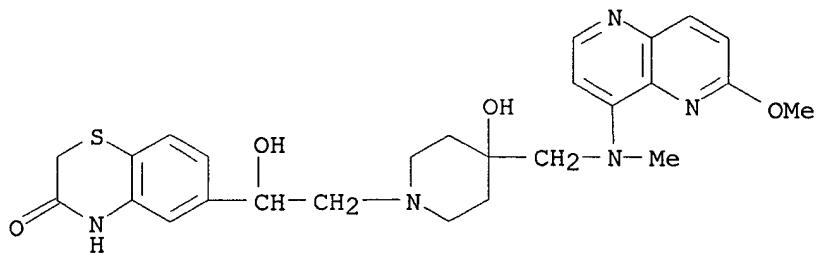
L7 ANSWER 5 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 495416-13-2 REGISTRY

CN 2H-1,4-Benzothiazin-3(4H)-one, 6-[1-hydroxy-2-[4-hydroxy-4-[(6-methoxy-1,5-naphthyridin-4-yl)methylamino]methyl]-1-piperidinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

MF C26 H31 N5 O4 S . 2 Cl H

SR CA  
LC STN Files: CA, CAPLUS

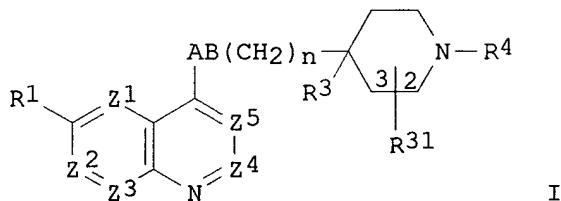


●2 HCl

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

GI



I

AB The title piperidine derivs. [I; one of Z1-Z5 is N, one is CR1a and the remainder are CH, or one or two of Z1-Z5 are independently CR1 a and the remainder are CH; R1, R1a = H, HO, C1-6 alkoxy optionally substituted by (un)substituted C1-6 alkoxy, amino, piperidyl, guanidino or amidino, C1-6 alkoxy-C1-6 alkyl, halo, C1-6 alkyl, C1-6 alkylthio, CF3, CF3O, etc.; R3 = CO2H, C1-6 alkoxycarbonyl, (un)substituted CONH2, cyano, tetrazolyl, (un)substituted 2-oxooxazolidinyl, 3-hydroxy-3-cyclobutene-1,2-dione-4-yl, 2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF3, C1-6 alkoxycarbonyl, C1-6 alkylcarbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenylcarbonyl,

(un)substituted OH or NH<sub>2</sub>, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH<sub>2</sub>R51, U-V-R52 (wherein R51 = C<sub>4</sub>-8 alkyl, hydroxy-C<sub>4</sub>-8 alkyl, C<sub>1</sub>-4 alkoxy-C<sub>4</sub>-8 alkyl, etc.; U = CO, SO<sub>2</sub>, CH<sub>2</sub> and V = (un)substituted CH<sub>2</sub>; or U = CH<sub>2</sub> and V = CO, (un)substituted C(:NOH), SO<sub>2</sub>; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH<sub>2</sub>, CH<sub>2</sub>CO, OCH<sub>2</sub>, CH<sub>2</sub>O, NHCH<sub>2</sub>, CH<sub>2</sub>NH, NH<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>] and pharmaceutically acceptable derivs. thereof are prep'd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K<sub>2</sub>CO<sub>3</sub> in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of .1toreq.4 .mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMC1, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

L7 ANSWER 6 OF 42 REGISTRY COPYRIGHT 2003 ACS

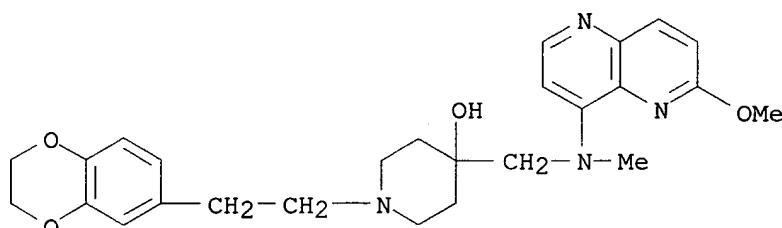
RN 495416-12-1 REGISTRY

CN 4-Piperidinol, 1-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]-4-[(6-methoxy-1,5-naphthyridin-4-yl)methylamino]methyl-, dihydrochloride (9CI) (CA INDEX NAME)

MF C26 H32 N4 O4 . 2 Cl H

SR CA

LC STN Files: CA, CAPLUS



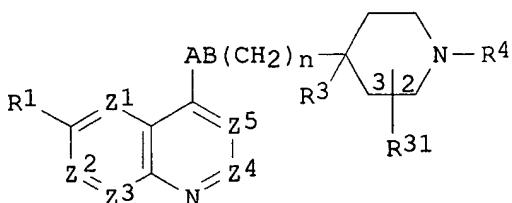
●2 HCl

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT,

LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

GI



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AB The title piperidine derivs. [I; one of Z1-Z5 is N, one is CR1a and the remainder are CH, or one or two of Z1-Z5 are independently CR1 a and the remainder are CH; R1, R1a = H, HO, C1-6 alkoxy optionally substituted by (un)substituted C1-6 alkoxy, amino, piperidyl, guanidino or amidino, C1-6 alkoxy-C1-6 alkyl, halo, C1-6 alkyl, C1-6 alkylthio, CF3, CF3O, etc.; R3 = CO2H, C1-6 alkoxycarbonyl, (un)substituted CONH2, cyano, tetrazolyl, (un)substituted 2-oxooxazolidinyl, 3-hydroxy-3-cyclobutene-1,2-dione-4-yl, 2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF3, C1-6 alkoxycarbonyl, C1-6 alkylcarbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenylcarbonyl, (un)substituted OH or NH2, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH2R51, U-V-R52 (wherein R51 = C4-8 alkyl, hydroxy-C4-8 alkyl, C1-4 alkoxy-C4-8 alkyl, etc.; U = CO, SO2, CH2 and V = (un)substituted CH2; or U = CH2 and V = CO, (un)substituted C(:NOH), SO2; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH2, CH2CO, OCH2, CH2O, NHCH2, CH2NH, NHSO2, CH2 SO2, CH2CH2] and pharmaceutically acceptable derivs. thereof are prepd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K2CO3 in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of .1toreq.4 .mu.g/mL against Staphylococcus aureus Oxford, S. aureus WCUH29, S. pneumoniae 1629, S. pneumoniae N1387, S. pneumoniae ERY 2, Enterococcus faecalis I, E. faecalis 7, Haemophilus influenzae Q1, H. influenzae NEMC1, Moraxella catarrhalis 1502, and Escherichia coli 7623.

L7 ANSWER 7 OF 42 REGISTRY COPYRIGHT 2003 ACS

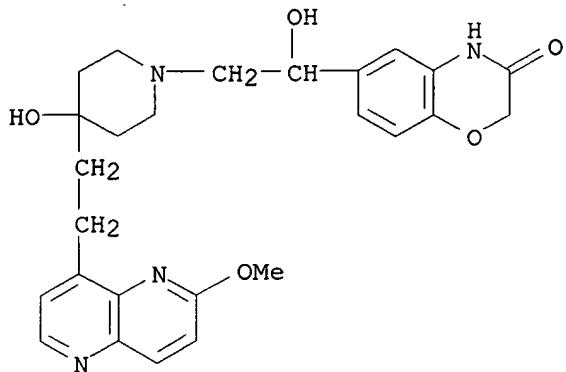
RN 495416-11-0 REGISTRY

CN 2H-1,4-Benzoxazin-3(4H)-one, 6-[1-hydroxy-2-[4-hydroxy-4-[2-(6-methoxy-1,5-naphthyridin-4-yl)ethyl]-1-piperidinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

INDEX NAME, MF C26 H30 N4 O5 2 C1 H

SB CA

LC STN Files: CA, CAPLUS

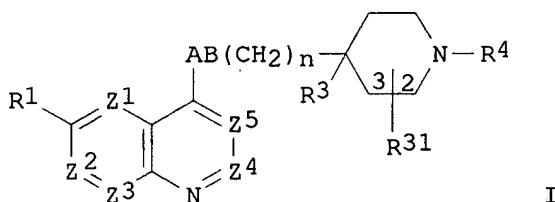


● 2 HCl

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

GI



I

AB The title piperidine derivs. [I; one of Z1-Z5 is N, one is CR1a and the remainder are CH, or one or two of Z1-Z5 are independently CR1 a and the remainder are CH; R1, R1a = H, HO, C1-6 alkoxy optionally substituted by (un)substituted C1-6 alkoxy, amino, piperidyl, guanidino or amidino, C1-6 alkoxy-C1-6 alkyl, halo, C1-6 alkyl, C1-6 alkylthio, CF<sub>3</sub>, CF<sub>3</sub>O, etc.; R3 = CO<sub>2</sub>H, C1-6 alkoxycarbonyl, (un)substituted CONH<sub>2</sub>, cyano, tetrazolyl, (un)substituted 2-oxooxazolidinyl, 3-hydroxy-3-cyclobutene-1,2-dione-4-yl, 2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF<sub>3</sub>, C1-6 alkoxycarbonyl, C1-6

alkylcarbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenylcarbonyl, (un)substituted OH or NH<sub>2</sub>, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH<sub>2</sub>R51, U-V-R52 (wherein R51 = C4-8 alkyl, hydroxy-C4-8 alkyl, C1-4 alkoxy-C4-8 alkyl, etc.; U = CO, SO<sub>2</sub>, CH<sub>2</sub> and V = (un)substituted CH<sub>2</sub>; or U = CH<sub>2</sub> and V = CO, (un)substituted C(:NOH), SO<sub>2</sub>; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH<sub>2</sub>, CH<sub>2</sub>CO, OCH<sub>2</sub>, CH<sub>2</sub>O, NHCH<sub>2</sub>, CH<sub>2</sub>NH, NH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>] and pharmaceutically acceptable derivs. thereof are prepd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K<sub>2</sub>CO<sub>3</sub> in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of 1toreq.4 .mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMC1, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

L7 ANSWER 8 OF 42 REGISTRY COPYRIGHT 2003 ACS

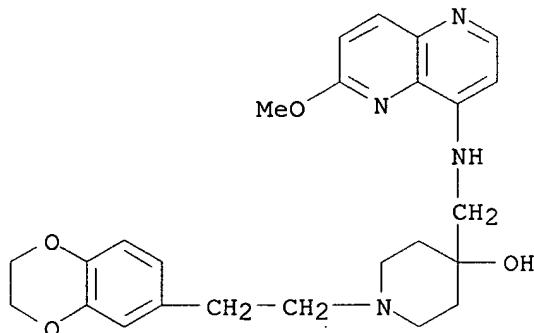
RN 495416-10-9 REGISTRY

CN 4-Piperidinol, 1-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]-4-[(6-methoxy-1,5-naphthyridin-4-yl)amino]methyl-, dihydrochloride (9CI) (CA INDEX NAME)

MF C25 H30 N4 O4 . 2 Cl H

SR CA

LC STN Files: CA, CAPLUS



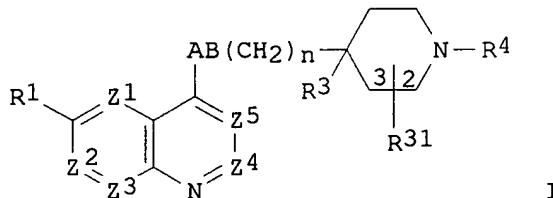
●2 HCl

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB,

GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

GI



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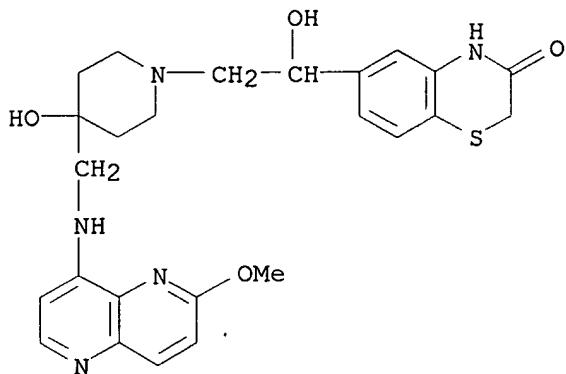
L7 ANSWER 9 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 495416-09-6 REGISTRY

CN 2H-1,4-Benzothiazin-3(4H)-one, 6-[1-hydroxy-2-[4-hydroxy-4-[(6-methoxy-1,5-naphthyridin-4-yl)amino]methyl]-1-piperidinyl]ethyl-, dihydrochloride (9CI) (CA INDEX NAME)

MF C25 H29 N5 O4 S . 2 Cl H

SR CA  
LC STN Files: CA, CAPLUS

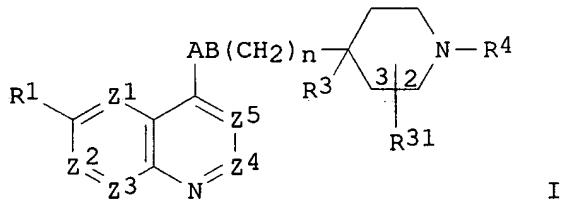


● 2 HCl

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

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2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF<sub>3</sub>, C1-6 alkoxy carbonyl, C1-6 alkylcarbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenylcarbonyl, (un)substituted OH or NH<sub>2</sub>, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH<sub>2</sub>R51, U-V-R52 (wherein R51 = C4-8 alkyl, hydroxy-C4-8 alkyl, C1-4 alkoxy-C4-8 alkyl, etc.; U = CO, SO<sub>2</sub>, CH<sub>2</sub> and V = (un)substituted CH<sub>2</sub>; or U = CH<sub>2</sub> and V = CO, (un)substituted C(:NOH), SO<sub>2</sub>; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH<sub>2</sub>, CH<sub>2</sub>CO, OCH<sub>2</sub>, CH<sub>2</sub>O, NHCH<sub>2</sub>, CH<sub>2</sub>NH, NHSO<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>] and pharmaceutically acceptable derivs. thereof are prep'd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K<sub>2</sub>CO<sub>3</sub> in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of .1 to req. 4 .mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMC1, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

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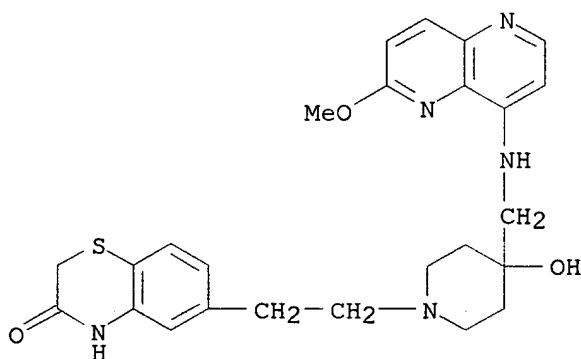
RN 495416-08-5 REGISTRY

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MF C25 H29 N5 O3 S . 2 Cl H

SR CA

LC STN Files: CA, CAPLUS



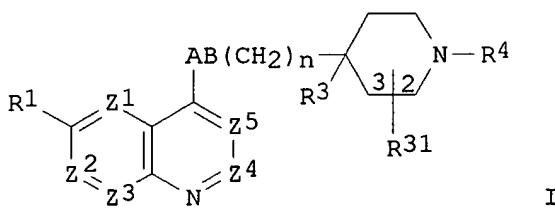
●2 HCl

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(Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206,  
97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,  
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB,  
GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US,  
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BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT,  
LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN:  
PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238  
20010726.

GI



AB The title piperidine derivs. [I; one of Z1-Z5 is N, one is CR1a and the remainder are CH, or one or two of Z1-Z5 are independently CR1 a and the remainder are CH; R1, R1a = H, HO, C1-6 alkoxy optionally substituted by (un)substituted C1-6 alkoxy, amino, piperidyl, guanidino or amidino, C1-6 alkoxy-C1-6 alkyl, halo, C1-6 alkyl, C1-6 alkylthio, CF3, CF3O, etc.; R3 = CO2H, C1-6 alkoxycarbonyl, (un)substituted CONH2, cyano, tetrazolyl, (un)substituted 2-oxooxazolidinyl, 3-hydroxy-3-cyclobutene-1,2-dione-4-yl, 2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF3, C1-6 alkoxycarbonyl, C1-6 alkylcarbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenylcarbonyl, (un)substituted OH or NH2, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH2R51, U-V-R52 (wherein R51 = C4-8 alkyl, hydroxy-C4-8 alkyl, C1-4 alkoxy-C4-8 alkyl, etc.; U = CO, SO2, CH2 and V = (un)substituted CH2; or U = CH2 and V = CO, (un)substituted C(:NOH), SO2; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH2, CH2CO, OCH2, CH2O, NHCH2, CH2NH, NHSO2, CH2 SO2, CH2CH2] and pharmaceutically acceptable derivs. thereof are prepd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K2CO3 in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of 1.1 to 1.4 .mu.g/mL against Staphylococcus aureus Oxford, S. aureus WCUH29, S. pneumoniae 1629, S. pneumoniae N1387, S. pneumoniae ERY 2, Enterococcus faecalis I, E. faecalis 7, Haemophilus influenzae Q1, H. influenzae NEMC1, Moraxella catarrhalis 1502, and Escherichia coli 7623.

L7 ANSWER 11 OF 42 REGISTRY COPYRIGHT 2003 ACS  
RN 495415-77-5 REGISTRY

CN 1,5-Naphthyridine, 8-[2-(4-fluoro-4-piperidinyl)ethyl]-2-methoxy- (9CI)  
(CA INDEX NAME)

OTHER NAMES:

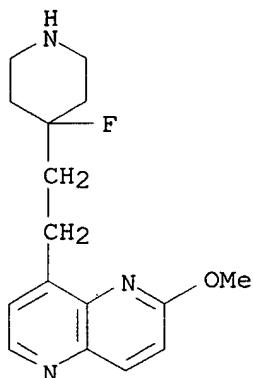
CN 8-[2-(4-Fluoropiperidin-4-yl)ethyl]-2-methoxy-[1,5]naphthyridine

FS 3D CONCORD

MF C16 H20 F N3 O

SR CA

LC STN Files: CA, CAPLUS

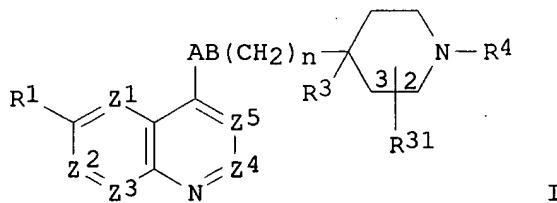


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L7 ANSWER 12 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 495415-73-1 REGISTRY

CN 2H-1,4-Benzothiazin-3(4H)-one, 6-[2-[4-fluoro-4-[2-(6-methoxy-1,5-naphthyridin-4-yl)ethyl]-1-piperidinyl]ethyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

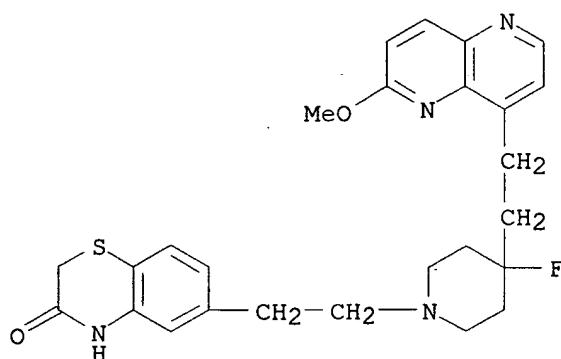
CN 6-[2-[4-Fluoro-4-[2-(6-methoxy-[1,5]naphthyridin-4-yl)ethyl]piperidin-1-yl]ethyl]-4H-benzo[1,4]thiazin-3-one

FS 3D CONCORD

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SR CA

LC STN Files: CA, CAPLUS

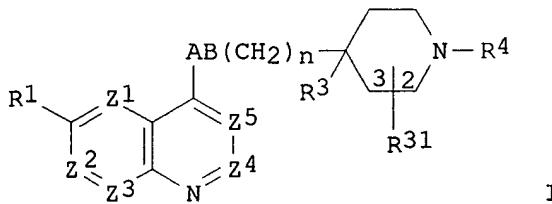


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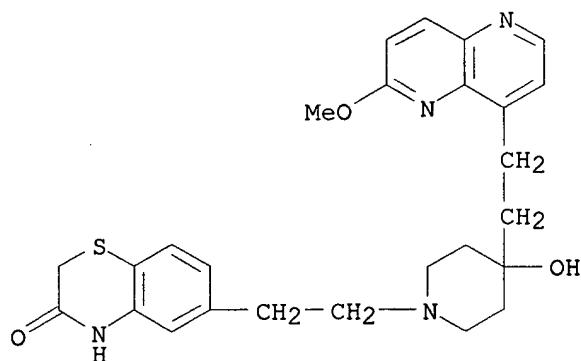


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.mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMC1, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

L7 ANSWER 13 OF 42 REGISTRY COPYRIGHT 2003 ACS  
RN 495415-69-5 REGISTRY  
CN 2H-1,4-Benzothiazin-3(4H)-one, 6-[2-[4-hydroxy-4-[2-(6-methoxy-1,5-naphthyridin-4-yl)ethyl]-1-piperidinyl]ethyl]- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
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FS 3D CONCORD  
MF C26 H30 N4 O3 S  
SR CA  
LC STN Files: CA, CAPLUS

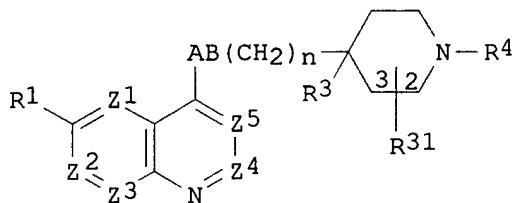


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AB The title piperidine derivs. [I; one of Z1-Z5 is N, one is CR1a and the remainder are CH, or one or two of Z1-Z5 are independently CR1 a and the remainder are CH; R1, R1a = H, HO, C1-6 alkoxy optionally substituted by (un)substituted C1-6 alkoxy, amino, piperidyl, guanidino or amidino, C1-6 alkoxy-C1-6 alkyl, halo, C1-6 alkyl, C1-6 alkylthio, CF3, CF3O, etc.; R3 = CO2H, C1-6 alkoxycarbonyl, (un)substituted CONH2, cyano, tetrazolyl, (un)substituted 2-oxooxazolidinyl, 3-hydroxy-3-cyclobutene-1,2-dione-4-yl, 2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF3, C1-6 alkoxycarbonyl, C1-6 alkylcarbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenylcarbonyl, (un)substituted OH or NH2, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH2R51, U-V-R52 (wherein R51 = C4-8 alkyl, hydroxy-C4-8 alkyl, C1-4 alkoxy-C4-8 alkyl, etc.; U = CO, SO2, CH2 and V = (un)substituted CH2; or U = CH2 and V = CO, (un)substituted C(:NOH), SO2; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH2, CH2CO, OCH2, CH2O, NHCH2, CH2NH, NHSO2, CH2 SO2, CH2CH2] and pharmaceutically acceptable derivs. thereof are prep'd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K2CO3 in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of 1toreq.4 .mu.g/mL against Staphylococcus aureus Oxford, S. aureus WCUH29, S. pneumoniae 1629, S. pneumoniae N1387, S. pneumoniae ERY 2, Enterococcus faecalis I, E. faecalis 7, Haemophilus influenzae Q1, H. influenzae NEMC1, Moraxella catarrhalis 1502, and Escherichia coli 7623.

L7 ANSWER 14 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 495415-67-3 REGISTRY

CN 4-Piperidinol, 4-[2-(6-methoxy-1,5-naphthyridin-4-yl)ethyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

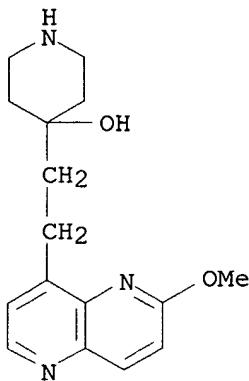
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FS 3D CONCORD

MF C16 H21 N3 O2

SR CA

LC STN Files: CA, CAPLUS

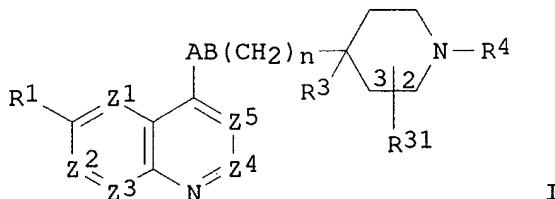


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

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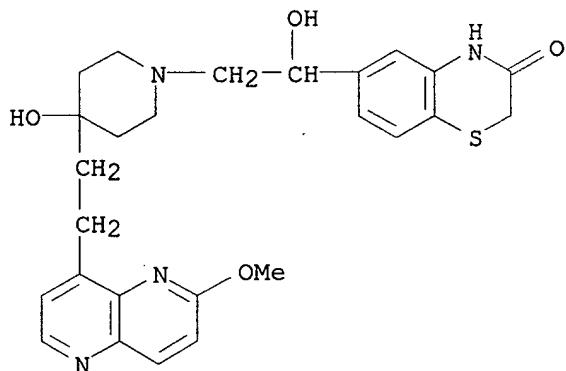


I

AB The title piperidine derivs. [I; one of Z1-Z5 is N, one is CR1a and the remainder are CH, or one or two of Z1-Z5 are independently CR1 a and the remainder are CH; R1, R1a = H, HO, C1-6 alkoxy optionally substituted by (un)substituted C1-6 alkoxy, amino, piperidyl, guanidino or amidino, C1-6 alkoxy-C1-6 alkyl, halo, C1-6 alkyl, C1-6 alkylthio, CF3, CF3O, etc.; R3 = CO2H, C1-6 alkoxy carbonyl, (un)substituted CONH2, cyano, tetrazolyl, (un)substituted 2-oxooxazolidinyl, 3-hydroxy-3-cyclobutene-1,2-dione-4-yl, 2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF3, C1-6 alkoxy carbonyl, C1-6 alkyl carbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenyl carbonyl,

(un)substituted OH or NH<sub>2</sub>, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH<sub>2</sub>R51, U-V-R52 (wherein R51 = C<sub>4</sub>-8 alkyl, hydroxy-C<sub>4</sub>-8 alkyl, C<sub>1</sub>-4 alkoxy-C<sub>4</sub>-8 alkyl, etc.; U = CO, SO<sub>2</sub>, CH<sub>2</sub> and V = (un)substituted CH<sub>2</sub>; or U = CH<sub>2</sub> and V = CO, (un)substituted C(:NOH), SO<sub>2</sub>; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH<sub>2</sub>, CH<sub>2</sub>CO, OCH<sub>2</sub>, CH<sub>2</sub>O, NHCH<sub>2</sub>, CH<sub>2</sub>NH, NH<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>] and pharmaceutically acceptable derivs. thereof are prep'd. These compds. are useful in methods of treatment of bacterial infections in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K<sub>2</sub>CO<sub>3</sub> in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of 1toreq.4 .mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMC1, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

L7 ANSWER 15 OF 42 REGISTRY COPYRIGHT 2003 ACS  
 RN 495415-63-9 REGISTRY  
 CN 2H-1,4-Benzothiazin-3(4H)-one, 6-[1-hydroxy-2-[4-hydroxy-4-[2-(6-methoxy-1,5-naphthyridin-4-yl)ethyl]-1-piperidinyl]ethyl]- (9CI) (CA INDEX NAME)  
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 MF C26 H30 N4 O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS



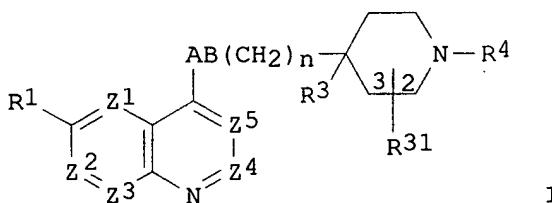
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB 2001-18238 20010726.

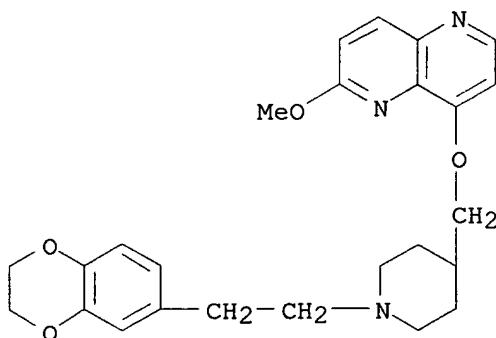
GI



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L7 ANSWER 16 OF 42 REGISTRY COPYRIGHT 2003 ACS  
 RN 477788-19-5 REGISTRY  
 CN 1,5-Naphthyridine, 8-[[1-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]-4-piperidinyl]methoxy]-2-methoxy- (9CI) (CA INDEX NAME)  
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 MF C25 H29 N3 O4  
 CI COM

SR CA  
LC STN Files: CA, CAPLUS

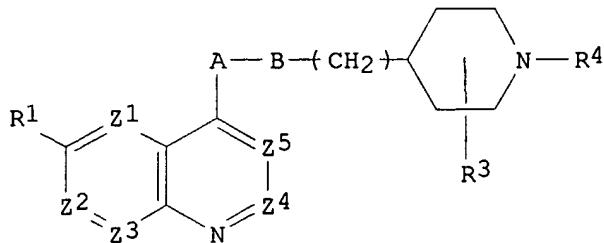


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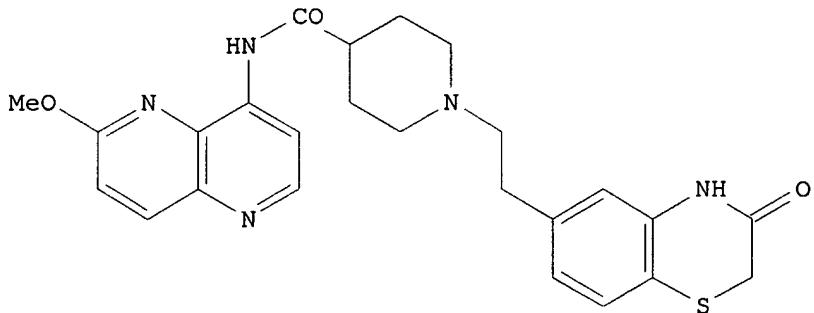
1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

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II

AB    Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = N, one is CR<sub>2</sub> (wherein R<sub>2</sub> = H, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, etc.) and the remainder are CH, or one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = CR<sub>2</sub> and the remainder are CH; R<sub>3</sub> = H, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R<sub>4</sub> = U-V-R<sub>5</sub>, wherein U-V = (CH<sub>2</sub>)<sub>2</sub>, CH<sub>2</sub>CH(OH), CH<sub>2</sub>CO, and R<sub>5</sub> is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prepd. For example, II was prepd. by a multistep synthetic procedure. The prepd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values  $\leq 4 \mu\text{g/mL}$  against *S. aureus* Oxford.

L7    ANSWER 17 OF 42    REGISTRY    COPYRIGHT 2003 ACS

RN    477788-18-4    REGISTRY

CN    2H-1,4-Benzothiazin-3(4H)-one, 6-[1-hydroxy-2-[4-[(6-methoxy-1,5-naphthyridin-4-yl)oxy]methyl]-1-piperidinyl]ethyl]-(9CI)    (CA INDEX NAME)

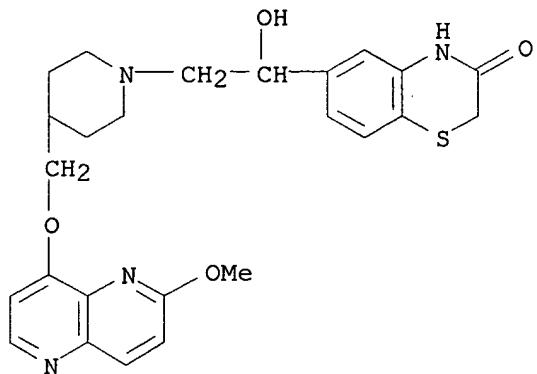
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MF    C25 H28 N4 O4 S

CI    COM

SR    CA

LC    STN Files:    CA, CAPLUS

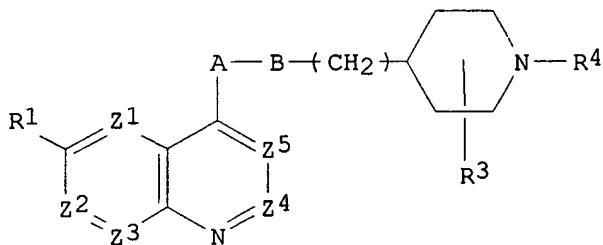


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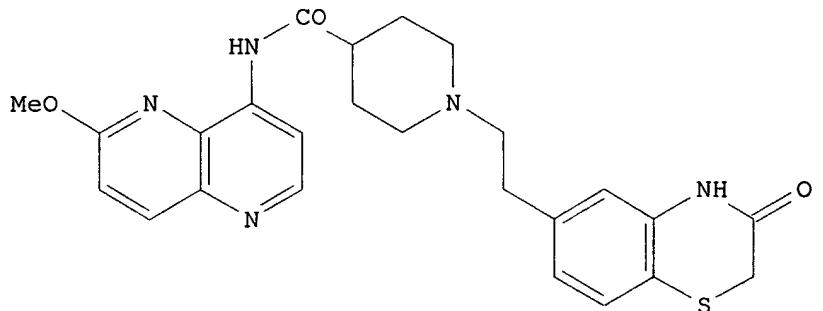
1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

GI



I



II

AB Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = N, one is CR<sub>2</sub> (wherein R<sub>2</sub> = H, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, etc.) and the remainder are CH, or one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = CR<sub>2</sub> and the remainder are CH; R<sub>3</sub> = H, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R<sub>4</sub> = U-V-R<sub>5</sub>, wherein U-V = (CH<sub>2</sub>)<sub>2</sub>, CH<sub>2</sub>CH(OH), CH<sub>2</sub>CO, and R<sub>5</sub> is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prep'd. For example, II was prep'd. by a multistep synthetic procedure. The prep'd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values  $\leq 4 \mu\text{g/mL}$  against *S. aureus* Oxford.

L7 ANSWER 18 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 477788-07-1 REGISTRY

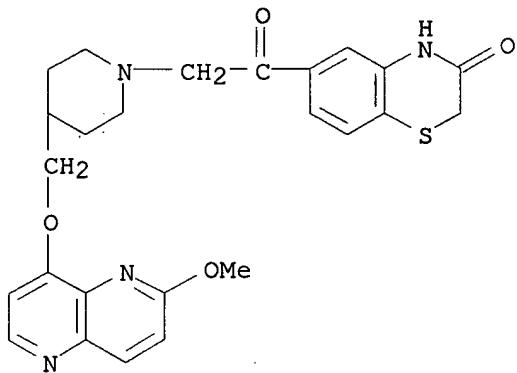
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FS 3D CONCORD

MF C25 H26 N4 O4 S

SR CA

LC STN Files: CA, CAPLUS

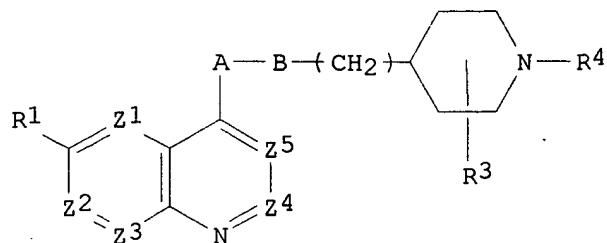


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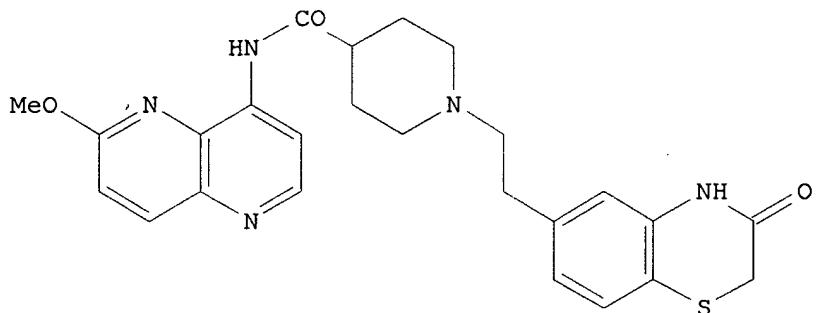
1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

GI



I



II

AB      Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = N, one is CR<sub>2</sub> (wherein R<sub>2</sub> = H, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, etc.) and the remainder are CH, or one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = CR<sub>2</sub> and the remainder are CH; R<sub>3</sub> = H, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R<sub>4</sub> = U-V-R<sub>5</sub>, wherein U-V = (CH<sub>2</sub>)<sub>2</sub>, CH<sub>2</sub>CH(OH), CH<sub>2</sub>CO, and R<sub>5</sub> is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prep'd. For example, II was prep'd. by a multistep synthetic procedure. The prep'd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values  $\leq 4 \mu\text{g/mL}$  against *S. aureus* Oxford.

L7      ANSWER 19 OF 42    REGISTRY    COPYRIGHT 2003 ACS

RN      477788-06-0    REGISTRY

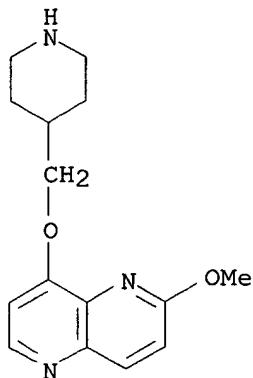
CN      1,5-Naphthyridine, 2-methoxy-8-(4-piperidinylmethoxy)- (9CI)    (CA INDEX NAME)

FS      3D CONCORD

MF      C15 H19 N3 O2

SR      CA

LC      STN Files:    CA, CAPLUS

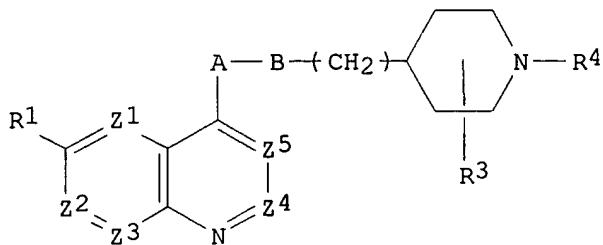


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

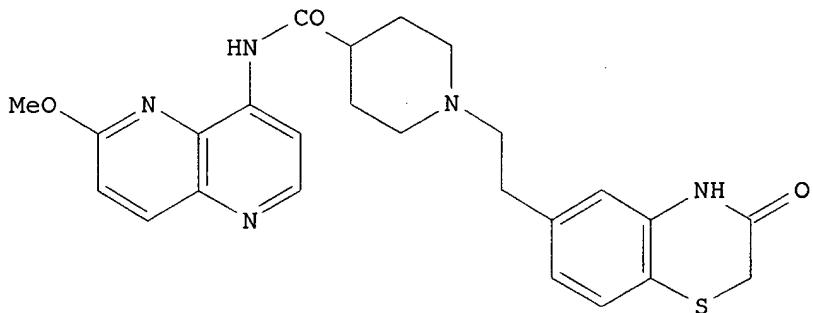
1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

GI



I



II

AB Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = N, one is CR<sub>2</sub> (wherein R<sub>2</sub> = H, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, etc.) and the remainder are CH, or one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = CR<sub>2</sub> and the remainder are CH; R<sub>3</sub> = H, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R<sub>4</sub> = U-V-R<sub>5</sub>, wherein U-V = (CH<sub>2</sub>)<sub>2</sub>, CH<sub>2</sub>CH(OH), CH<sub>2</sub>CO, and R<sub>5</sub> is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prepd. For example, II was prepd. by a multistep synthetic procedure. The prepd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values  $\leq 4 \mu\text{g/mL}$  against *S. aureus* Oxford.

L7 ANSWER 20 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 477788-05-9 REGISTRY

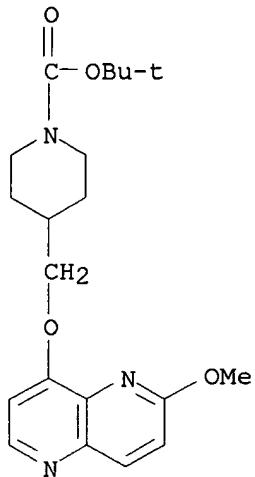
CN 1-Piperidinecarboxylic acid, 4-[[[6-methoxy-1,5-naphthyridin-4-yl)oxymethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H27 N3 O4

SR CA

LC STN Files: CA, CAPLUS

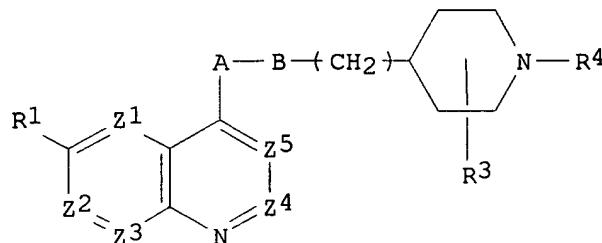


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

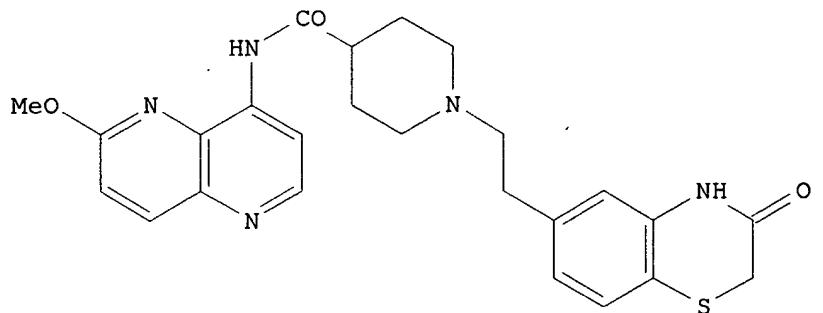
1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

GI



I



II

AB    Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = N, one is CR<sub>2</sub> (wherein R<sub>2</sub> = H, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, etc.) and the remainder are CH, or one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = CR<sub>2</sub> and the remainder are CH; R<sub>3</sub> = H, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R<sub>4</sub> = U-V-R<sub>5</sub>, wherein U-V = (CH<sub>2</sub>)<sub>2</sub>, CH<sub>2</sub>CH(OH), CH<sub>2</sub>CO, and R<sub>5</sub> is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prep'd. For example, II was prep'd. by a multistep synthetic procedure. The prep'd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values .1 to < 4 .μ.g/mL against S. aureus Oxford.

L7    ANSWER 21 OF 42    REGISTRY    COPYRIGHT 2003 ACS

RN    477787-59-0    REGISTRY

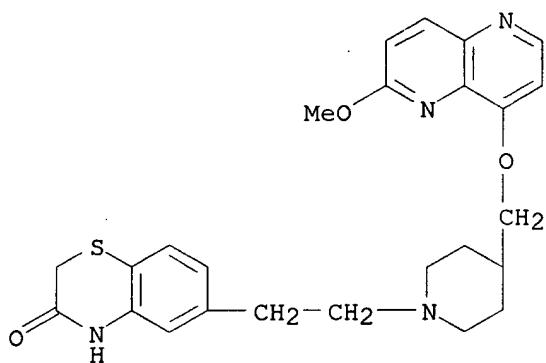
CN    2H-1,4-Benzothiazin-3(4H)-one, 6-[2-[4-[[[6-methoxy-1,5-naphthyridin-4-yl)oxy]methyl]-1-piperidinyl]ethyl]- (9CI)    (CA INDEX NAME)

FS    3D CONCORD

MF    C25 H28 N4 O3 S

SR    CA

LC    STN Files:    CA, CAPLUS

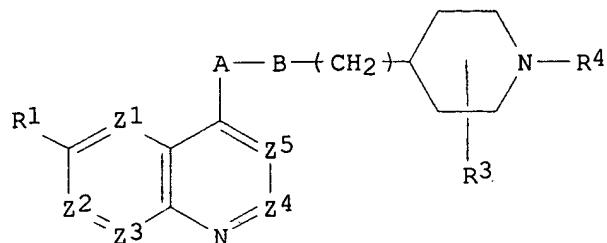


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

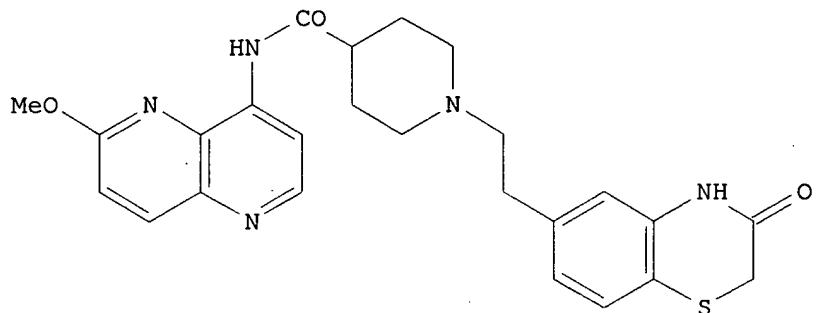
1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

GI



I



II

AB    Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = N, one is CR<sub>2</sub> (wherein R<sub>2</sub> = H, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, etc.) and the remainder are CH, or one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = CR<sub>2</sub> and the remainder are CH; R<sub>3</sub> = H, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R<sub>4</sub> = U-V-R<sub>5</sub>, wherein U-V = (CH<sub>2</sub>)<sub>2</sub>, CH<sub>2</sub>CH(OH), CH<sub>2</sub>CO, and R<sub>5</sub> is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prep'd. For example, II was prep'd. by a multistep synthetic procedure. The prep'd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values .1 to < 4  $\mu$ g/mL against S. aureus Oxford.

L7    ANSWER 22 OF 42    REGISTRY    COPYRIGHT 2003 ACS

RN    477787-57-8    REGISTRY

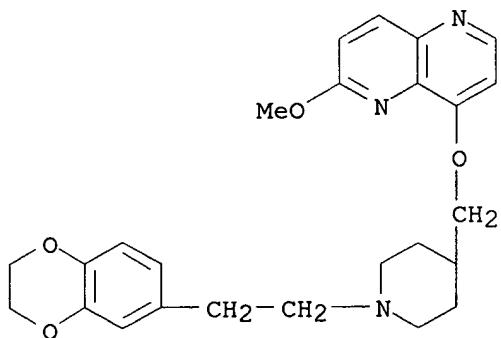
CN    1,5-Naphthyridine, 8-[[1-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]-4-piperidinyl]methoxy]-2-methoxy-, hydrochloride (9CI)    (CA INDEX NAME)

MF    C<sub>25</sub> H<sub>29</sub> N<sub>3</sub> O<sub>4</sub> . x Cl H

SR    CA

LC    STN Files:    CA, CAPLUS

CRN    (477788-19-5)

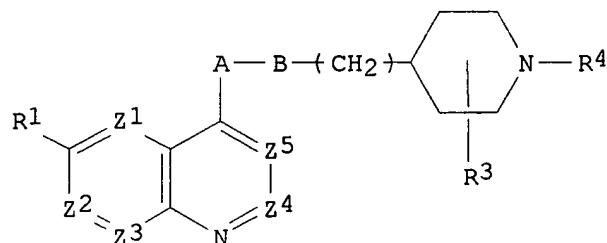


● x HCl

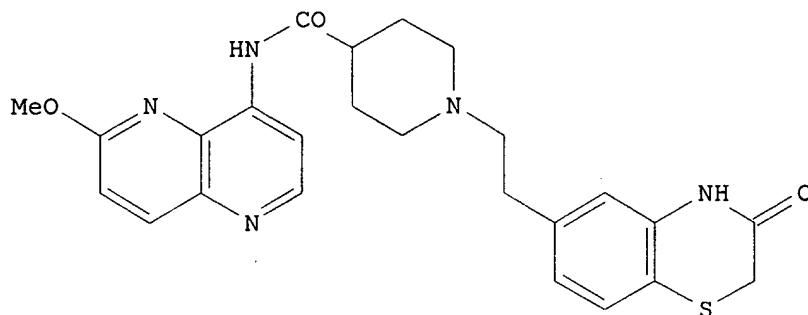
1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

GI



I



II

AB Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = N, one is CR<sub>2</sub> (wherein R<sub>2</sub> = H, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, etc.) and the remainder are CH, or one of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> = CR<sub>2</sub> and the remainder are CH; R<sub>3</sub> = H, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R<sub>4</sub> = U-V-R<sub>5</sub>, wherein U-V = (CH<sub>2</sub>)<sub>2</sub>, CH<sub>2</sub>CH(OH), CH<sub>2</sub>CO, and R<sub>5</sub> is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prepd. For example, II was prepd. by a multistep synthetic procedure. The prepd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values .1 to < 4 .μ.g/mL against S. aureus Oxford.

L7 ANSWER 23 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 477787-45-4 REGISTRY

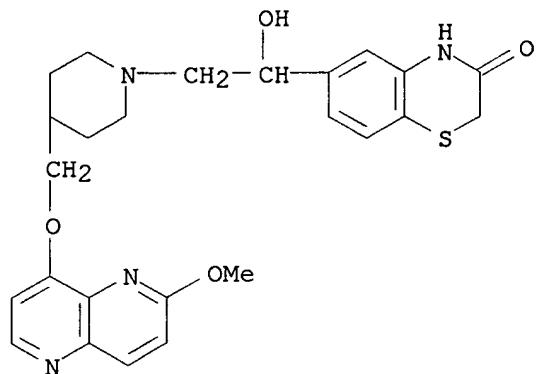
CN 2H-1,4-Benzothiazin-3(4H)-one, 6-[1-hydroxy-2-[4-[(6-methoxy-1,5-dihydro-4H-thiazin-3(4H)-one)oxy]methyl]-1-piperidinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

MF C25 H28 N4 O4 S . x Cl H

SR CA

LC STN Files: CA, CAPLUS

CRN (477788-18-4)

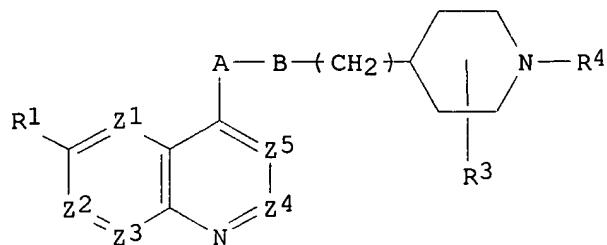


●x HCl

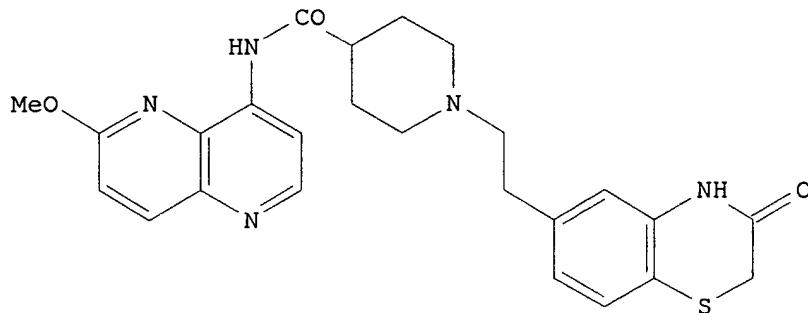
1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

GI



I



II

AB    Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z1, Z2, Z3, Z4, Z5 = N, one is CR2 (wherein R2 = H, OH, (C1-C6)alkoxy, etc.) and the remainder are CH, or one of Z1, Z2, Z3, Z4, Z5 = CR2 and the remainder are CH; R3 = H, carboxy, (C1-C6)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R4 = U-V-R5, wherein U-V = (CH2)2, CH2CH(OH), CH2CO, and R5 is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prepd. For example, II was prepd. by a multistep synthetic procedure. The prepd. compds. are useful in the treatment of bacterial infections in mammals, particularly man. For example, compd. II had MIC values  $\leq 4 \mu\text{g/mL}$  against *S. aureus* Oxford.

L7    ANSWER 24 OF 42    REGISTRY    COPYRIGHT 2003 ACS

RN    405933-83-7    REGISTRY

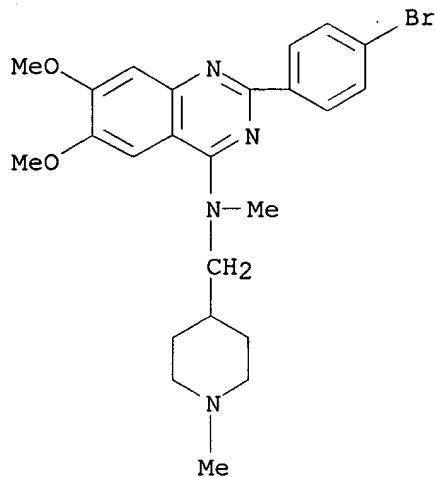
CN    4-Quinazolinamine, 2-(4-bromophenyl)-6,7-dimethoxy-N-methyl-N-[(1-methyl-4-piperidinyl)methyl]- (9CI)    (CA INDEX NAME)

FS    3D CONCORD

MF    C24 H29 Br N4 O2

SR    CA

LC    STN Files:    CA, CAPLUS

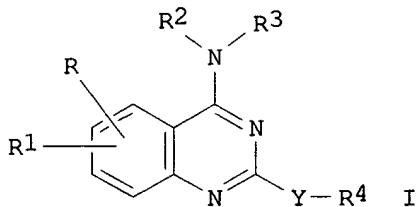


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:279468 Preparation of 4-amino-quinazolines useful as glycoprotein IbIX antagonists, and their use for control of thrombotic disorders. Mederski, Werner; Devant, Ralf; Barnickel, Gerhard; Bernotat-Danielowski, Sabine; Vickers, James; Cezanne, Bertram; Dhanoa, Daljit; Zhao, Bao-Ping; Rinker, James; Player, Mark R.; Jaeger, Edward; Soll, Richard (Merck Patent G.m.b.H., Germany). PCT Int. Appl. WO 2002024667 A1 20020328, 83 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP10705 20010917. PRIORITY: US 2000-666908 20000920.

GI



AB The prepn. of 4-amino-quinazolines [I; wherein R, R1, independently = H, (C1-C6)alkyl, OH, (C1-C6)alkoxy, amino, nitro, cyano, etc.; R2, R3, independently = H, (C1-C6)alkyl, cycloalkyl, mono- or bicycloheterocyclic

radical, etc.; R4 = aryl (e.g., Ph, naphthyl, biphenyl, etc.), or thiophen-2-yl substituted with aryl (as described supra) or heterocyclic radical, etc.; each of R, R1-R4 with many provisos] is described. Thus, [2-(4-bromophenyl)-7-chloroquinazolin-4-yl]-phenylamine was prepd. by a multistep synthesis. The prepd. compds. are useful as glycoprotein IbIX antagonists (no data) for the control of thrombotic disorders and sequelae deriving thereof.

L7 ANSWER 25 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 405933-55-3 REGISTRY

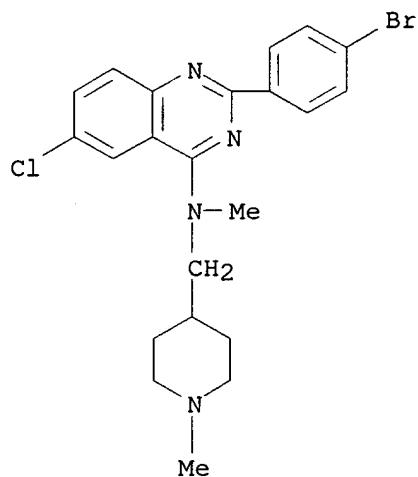
CN 4-Quinazolinamine, 2-(4-bromophenyl)-6-chloro-N-methyl-N-[(1-methyl-4-piperidinyl)methyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H24 Br Cl N4

SR CA

LC STN Files: CA, CAPLUS



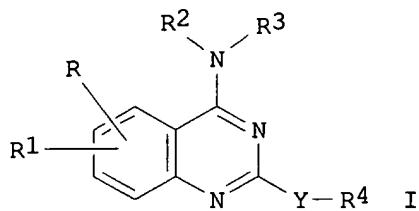
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:279468 Preparation of 4-amino-quinazolines useful as glycoprotein IbIX antagonists, and their use for control of thrombotic disorders. Mederski, Werner; Devant, Ralf; Barnickel, Gerhard; Bernotat-Danielowski, Sabine; Vickers, James; Cezanne, Bertram; Dhanoa, Daljit; Zhao, Bao-Ping; Rinker, James; Player, Mark R.; Jaeger, Edward; Soll, Richard (Merck Patent G.m.b.H., Germany). PCT Int. Appl. WO 2002024667 A1 20020328, 83 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP10705 20010917. PRIORITY: US 2000-666908 20000920.

GI



AB The prepn. of 4-amino-quinazolines [I; wherein R, R1, independently = H, (C1-C6)alkyl, OH, (C1-C6)alkoxy, amino, nitro, cyano, etc.; R2,R3, independently = H, (C1-C6)alkyl, cycloalkyl, mono- or bicycloheterocyclic radical, etc.; R4 = aryl (e.g., Ph, naphthyl, biphenyl, etc.), or thiophen-2-yl substituted with aryl (as described *supra*) or heterocyclic radical, etc.; each of R, R1-R4 with many provisos] is described. Thus, [2-(4-bromophenyl)-7-chloroquinazolin-4-yl]-phenylamine was prepd. by a multistep synthesis. The prepd. compds. are useful as glycoprotein IbIX antagonists (no data) for the control of thrombotic disorders and sequelae deriving thereof.

L7 ANSWER 26 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 405933-37-1 REGISTRY

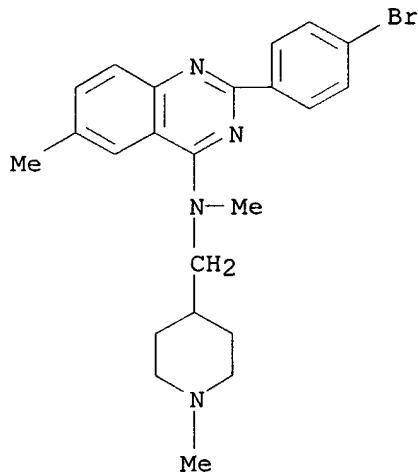
CN 4-Quinazolinamine, 2-(4-bromophenyl)-N,6-dimethyl-N-[(1-methyl-4-piperidinyl)methyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C23 H27 Br N4

SR CA

LC STN Files: CA, CAPLUS



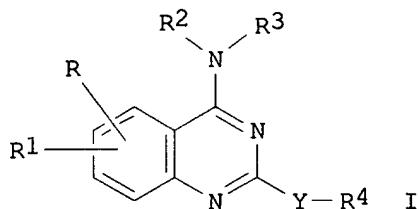
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:279468 Preparation of 4-amino-quinazolines useful as glycoprotein IbIX antagonists, and their use for control of thrombotic disorders. Mederski, Werner; Devant, Ralf; Barnickel, Gerhard; Bernotat-Danielowski, Sabine; Vickers, James; Cezanne, Bertram; Dhanoa, Daljit; Zhao, Bao-Ping; Rinker, James; Player, Mark R.; Jaeger, Edward; Soll, Richard (Merck Patent G.m.b.H., Germany). PCT Int. Appl. WO 2002024667 A1 20020328, 83 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP10705 20010917. PRIORITY: US 2000-666908 20000920.

GI



AB The prepn. of 4-amino-quinazolines [I; wherein R, R<sub>1</sub>, independently = H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, amino, nitro, cyano, etc.; R<sub>2</sub>, R<sub>3</sub>, independently = H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, cycloalkyl, mono- or bicycloheterocyclic radical, etc.; R<sub>4</sub> = aryl (e.g., Ph, naphthyl, biphenyl, etc.), or thiophen-2-yl substituted with aryl (as described supra) or heterocyclic radical, etc.; each of R, R<sub>1</sub>-R<sub>4</sub> with many provisos] is described. Thus, [2-(4-bromophenyl)-7-chloroquinazolin-4-yl]-phenylamine was prepd. by a multistep synthesis. The prepd. compds. are useful as glycoprotein IbIX antagonists (no data) for the control of thrombotic disorders and sequelae deriving thereof.

L7 ANSWER 27 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 387347-06-0 REGISTRY

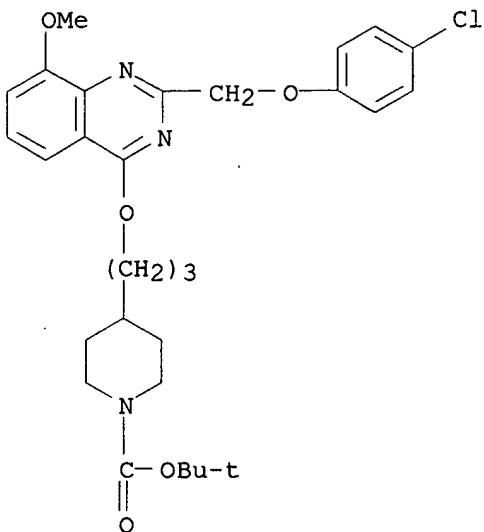
CN 1-Piperidinecarboxylic acid, 4-[3-[[2-[(4-chlorophenoxy)methyl]-8-methoxy-4-quinazolinyl]oxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C29 H36 Cl N3 O5

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

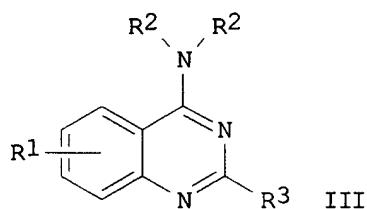
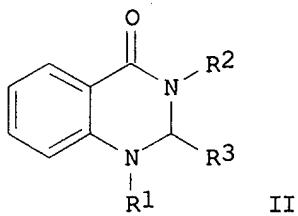
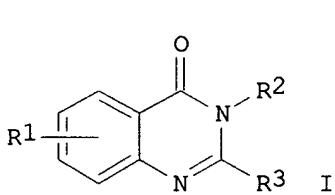


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:85820 Preparation of quinazolines and quinazolinones as neuropeptide Y receptor antagonists for treatment of obesity and circulatory disorders. Carpino, Philip A. (Pfizer Inc., USA). U.S. US 6337332 B1 20020108, 24 pp. (English). CODEN: USXXAM. APPLICATION: US 1999-382418 19990824. PRIORITY: US 1998-PV100749 19980917.

GI



AB Title compds. (I, II, and III) [wherein R1 = (halo)methyl, OMe, or halo; R2 = H, (un)substituted piperidinylpropyl or piperazinylpropyl, (halo)phenylpropyl, or pyridinylpropyl; R3 = Me, (halo)styryl, or (halo)phenoxyethyl; and pharmaceutically acceptable salts thereof] were

prep'd. as neuropeptide Y antagonists. For example, a soln. of 4-chlorophenoxyacetyl chloride in toluene was added to a soln. of 2-amino-3-methoxybenzoic acid and DMAP in pyridine and stirred for 17 h at 5.degree.C to give a mixt. of 2-[2-(4-chlorophenoxy)acetylamino]-3-methoxybenzoic acid and 2-(4-chlorophenoxyethyl)-8-methoxybenzo[*d*][1,3]oxazin-4-one. The mixt. was heated to 150.degree.C in formamide for 17 h and cooled to room temp. to afford 2-(4-chlorophenoxyethyl)-8-methoxy-3*H*-quinazolin-4-one. The invention compds. are useful for the treatment of obesity and circulatory disorders (no data).

L7 ANSWER 28 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 264232-54-4 REGISTRY

CN 1,5-Naphthyridine-4-ethanol, .alpha.-[(3*R*,4*S*)-3-ethenyl-1-heptyl-4-piperidinylmethyl]-6-methoxy- (9CI) (CA INDEX NAME)

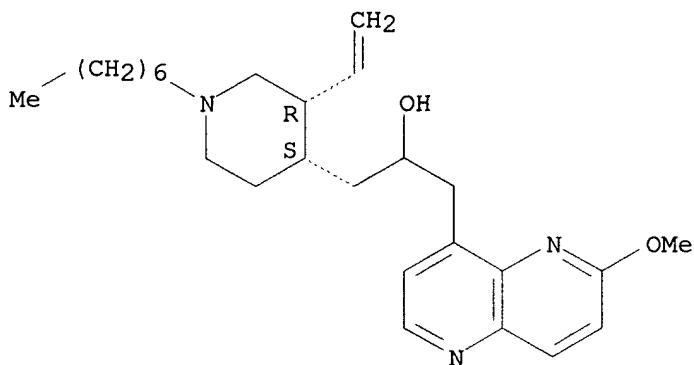
FS STEREOSEARCH

MF C26 H39 N3 O2

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



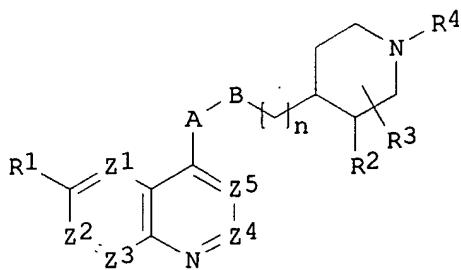
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:293679 Preparation of naphthyridines and their azaisosteric analogues as antibacterials. Hatton, Ian Keith; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2000021948 A1 20000420, 38 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB3366 19991011. PRIORITY: GB 1998-22450 19981014.

GI



AB The title compds. [I; one of Z1-Z5 = N and the remainder are CH; R1 = H, OH, alkoxy, etc.; either R2 = H, and R3 is in the 2- or 3-position and is H, alkyl, alkenyl, etc.; or R3 is in the 3-position and R2 and R3 together are a divalent :CR6R7 (wherein R6 and R7 = H, alkyl, alkenyl, etc.); R4 = CH2R5 (R5 = alkyl, hydroxyalkyl, alkoxyalkyl, etc.); n = 0-2; A, B = NR8, O, SOx, etc.; x = 0-2; R8 = H, CF3, alkyl, etc.] and their pharmaceutically acceptable derivs., useful in the treatment of bacterial infections in mammals, particularly in man, were prep'd. E.g., a multi-step synthesis of (3R,4S)-I [Z1-Z4 = CH; Z5 = N; R1 = OMe; A = N(Me); B = CH2; n = 1; R2 = CH:CH2; R3 = H; R4 = n-heptyl] which showed MIC of 0.5 .mu.g/mL against S. aureus Oxford, M. catarrhalis Rivasio and S. pneumoniae, was given.

L7 ANSWER 29 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 264232-49-7 REGISTRY

CN Quinazoline, 4-[2-[(3R,4S)-3-ethenyl-1-heptyl-4-piperidinyl]ethoxy]-6-methoxy- (9CI) (CA INDEX NAME)

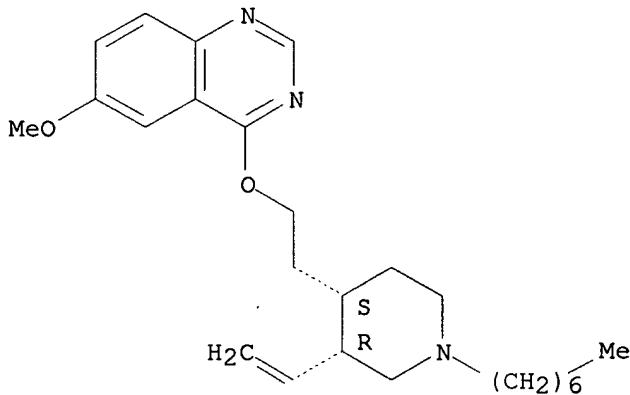
FS STEREOSEARCH

MF C25 H37 N3 O2

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

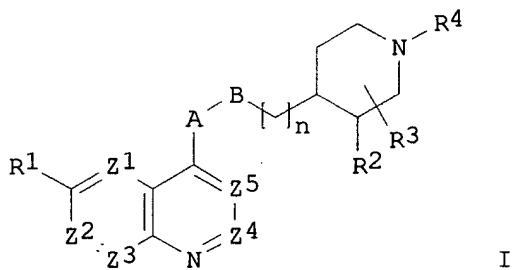
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:293679 Preparation of naphthyridines and their azaisosteric

Searched by: Mary Hale 308-4258 CM-1 1E01

analogues as antibacterials. Hatton, Ian Keith; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2000021948 A1 20000420, 38 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB3366 19991011. PRIORITY: GB 1998-22450 19981014.

GI



AB The title compds. [I; one of Z1-Z5 = N and the remainder are CH; R1 = H, OH, alkoxy, etc.; either R2 = H, and R3 is in the 2- or 3-position and is H, alkyl, alkenyl, etc.; or R3 is in the 3-position and R2 and R3 together are a divalent :CR6R7 (wherein R6 and R7 = H, alkyl, alkenyl, etc.); R4 = CH2R5 (R5 = alkyl, hydroxyalkyl, alkoxyalkyl, etc.); n = 0-2; A, B = NR8, O, SOx, etc.; x = 0-2; R8 = H, CF3, alkyl, etc.] and their pharmaceutically acceptable derivs., useful in the treatment of bacterial infections in mammals, particularly in man, were prep'd. E.g., a multi-step synthesis of (3R,4S)-I [Z1-Z4 = CH; Z5 = N; R1 = OMe; A = N(Me); B = CH2; n = 1; R2 = CH:CH2; R3 = H; R4 = n-heptyl] which showed MIC of 0.5 .mu.g/mL against S. aureus Oxford, M. catarrhalis Ravasio and S. pneumoniae, was given.

L7 ANSWER 30 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 264232-48-6 REGISTRY

CN 4-Quinazolinamine, N-[2-[(3R,4S)-3-ethenyl-1-heptyl-4-piperidinyl]ethyl]-6-methoxy-N-methyl- (9CI) (CA INDEX NAME)

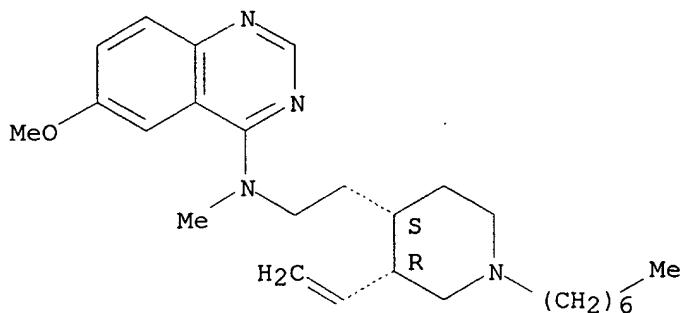
FS STEREOSEARCH

MF C26 H40 N4 O

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

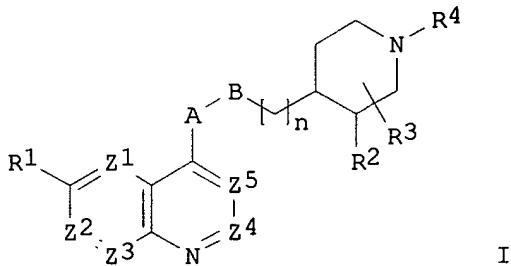


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

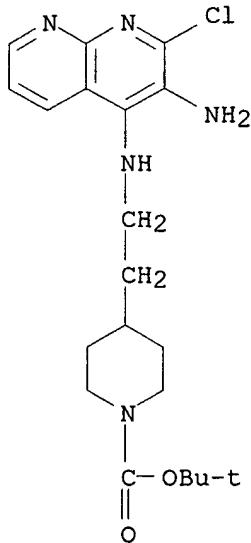
REFERENCE 1: 132:293679 Preparation of naphthyridines and their azaisosteric analogues as antibacterials. Hatton, Ian Keith; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2000021948 A1 20000420, 38 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB3366 19991011. PRIORITY: GB 1998-22450 19981014.

GI



AB The title compds. [I; one of Z1-Z5 = N and the remainder are CH; R1 = H, OH, alkoxy, etc.; either R2 = H, and R3 is in the 2- or 3-position and is H, alkyl, alkenyl, etc.; or R3 is in the 3-position and R2 and R3 together are a divalent :CR6R7 (wherein R6 and R7 = H, alkyl, alkenyl, etc.); R4 = CH2R5 (R5 = alkyl, hydroxyalkyl, alkoxyalkyl, etc.); n = 0-2; A, B = NR8, O, SOx, etc.; x = 0-2; R8 = H, CF3, alkyl, etc.] and their pharmaceutically acceptable derivs., useful in the treatment of bacterial infections in mammals, particularly in man, were prep'd. E.g., a multi-step synthesis of (3R,4S)-I [Z1-Z4 = CH; Z5 = N; R1 = OMe; A = N(Me); B = CH2; n = 1; R2 = CH:CH2; R3 = H; R4 = n-heptyl] which showed MIC of 0.5 .mu.g/mL against S. aureus Oxford, M. catarrhalis Ravasio and S. pneumoniae, was given.

L7 ANSWER 31 OF 42 REGISTRY COPYRIGHT 2003 ACS  
RN 259181-22-1 REGISTRY  
CN 1-Piperidinecarboxylic acid, 4-[2-[(3-amino-2-chloro-1,8-naphthyridin-4-yl)amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H28 Cl N5 O2  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

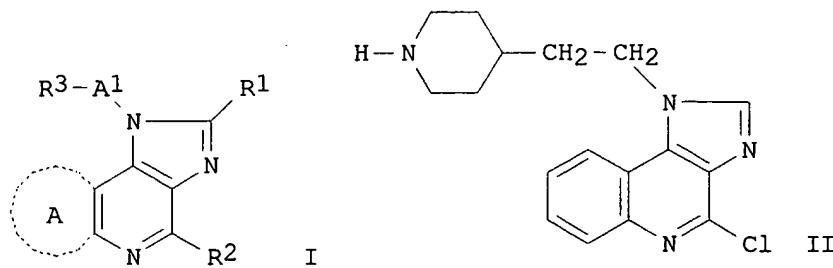


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:180573 Preparation of imidazopyridine derivatives as TNF and IL-1 production inhibitors. Kato, Hideo; Sakaguchi, Jun; Aoyama, Makoto; Izumi, Tomoyuki; Kato, Ken-ichi (Hokuriku Seiyaku Co., Ltd., Japan). PCT Int. Appl. WO 2000009506 A1 20000224, 111 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1999-JP4381 19990812. PRIORITY: JP 1998-241062 19980812; JP 1999-216125 19990730.

GI



AB The title compds. I [A1 = (CH<sub>2</sub>)<sub>m</sub>; R1 is hydrogen, hydroxyl, alkyl, cycloalkyl, styryl or aryl; R2 is hydrogen, alkyl, halogeno, hydroxyl, amino, cyclic amino or phenoxy; ring A is an optionally substituted homocycle or heterocycle; R3 is a satd. nitrogenous heterocyclic group; and m is an integer of 0 to 3] are prep'd. In an in vitro test using cells, the title compd. II.CF<sub>3</sub>CO<sub>2</sub>H at 0.001 .mu.mol gave 79% inhibition of TNF-.alpha. prodn.

L7 ANSWER 32 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 259180-95-5 REGISTRY

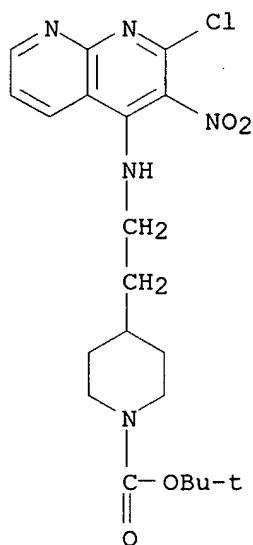
CN 1-Piperidinocarboxylic acid, 4-[2-[(2-chloro-3-nitro-1,8-naphthyridin-4-yl)amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H26 C1 N5 O4

SR CA

LC STN Files: CA, CAPLUS, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

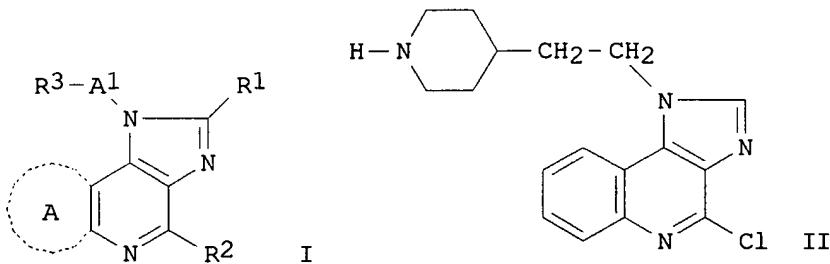
1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:180573 Preparation of imidazopyridine derivatives as TNF and IL-1 production inhibitors. Kato, Hideo; Sakaguchi, Jun; Aoyama,

Searched by: Mary Hale 308-4258 CM-1 1E01

Makoto; Izumi, Tomoyuki; Kato, Ken-ichi (Hokuriku Seiyaku Co., Ltd., Japan). PCT Int. Appl. WO 2000009506 A1 20000224, 111 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1999-JP4381 19990812. PRIORITY: JP 1998-241062 19980812; JP 1999-216125 19990730.

GI



AB The title compds. I [A1 = (CH<sub>2</sub>)<sub>m</sub>; R1 is hydrogen, hydroxyl, alkyl, cycloalkyl, styryl or aryl; R2 is hydrogen, alkyl, halogeno, hydroxyl, amino, cyclic amino or phenoxy; ring A is an optionally substituted homocycle or heterocycle; R3 is a satd. nitrogenous heterocyclic group; and m is an integer of 0 to 3] are prep'd. In an in vitro test using cells, the title compd. II.CF<sub>3</sub>CO<sub>2</sub>H at 0.001 .mu.mol gave 79% inhibition of TNF-.alpha. prodn.

L7 ANSWER 33 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 240427-22-9 REGISTRY

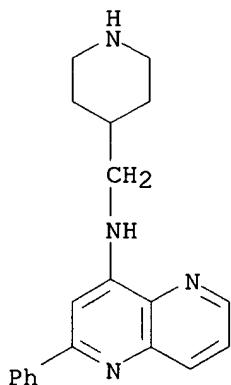
CN 1,5-Naphthyridin-4-amine, 2-phenyl-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H22 N4

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

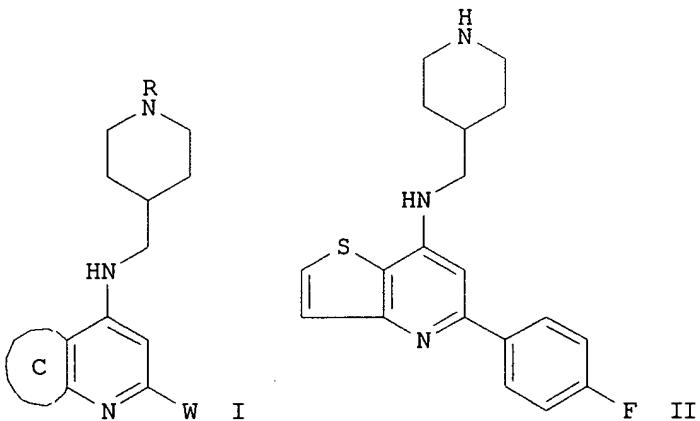


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 131:184940 Preparation of N-(4-piperidinylmethyl)thieno[3,2-b]pyridin-7-amines and related compounds as GABA brain receptor ligands. Cai, Guolin; Liu, Gang (Neurogen Corporation, USA). PCT Int. Appl. WO 9943681 A1 19990902, 39 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US4185 19990226. PRIORITY: US 1998-PV76006 19980226.

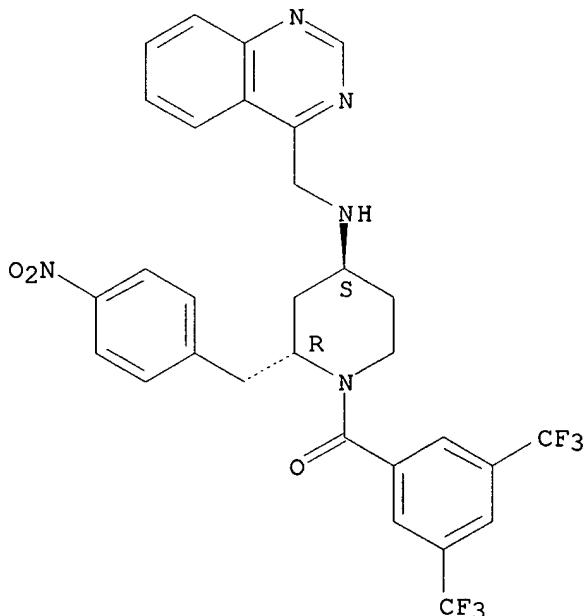
GI



AB The title compds. [I; ring C is (un)substituted thiophene, pyridine, pyrazine, pyridazine, pyrimidine ring; R = H, (hydroxy)C1-6 alkyl, amino(C1-6) alkyl, CONR1R2, etc.; R1, R2 = H, alkyl; W = (un)substituted (hetero)aryl, 2-, 3-thienyl, 2-, 3-, 4-pyridyl, CONR3R4; R3, R4 = alkyl] or their pharmaceutically acceptable nontoxic salts, highly selective agonists, antagonists or inverse agonists for GABAA brain receptors or their prodrugs, were prep'd. and 8 specific I are claimed. I have  $K_i < 200$  for GABAA receptor binding in vitro and are useful in the diagnosis and treatment of anxiety, Down's syndrome, sleep, cognitive and seizure disorders, and overdose with benzodiazepine drugs and for enhancement of alertness. For example, refluxing 8 g 3-amino-2-thiophenecarboxylic acid and 9.6 g 4-FC6H4COCH2CO2Et for 20 h in 100 mL PhMe in the presence of 0.2 g p-MeC6H4SO3H.cntdot.H2O with removal of H2O gave a solid which was dissolved in 80 mL Ph2O and heated for 2 h at 220.degree. to give 2 g 5-(4-fluorophenyl)thieno[3,2-b]pyridin-7-ol m. 316-318.degree.. This alc. (1.6 g) was refluxed for 3 h in 50 mL POCl3 to give 1.5 g of the appropriate chloride which (60 mg) was heated for 4 h at 160.degree. with 1 mL 4-(aminomethyl)piperidine under N to give a title compd. II.

L7 ANSWER 34 OF 42 REGISTRY COPYRIGHT 2003 ACS  
RN 200641-62-9 REGISTRY  
CN 4-Piperidinamine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(4-nitrophenyl)methyl]-N-(4-quinazolinylmethyl)-, (2R-trans)- (9CI) (CA  
INDEX NAME)  
FS STEREOSEARCH  
MF C30 H25 F6 N5 O3  
SR CA  
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

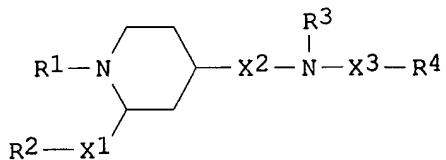


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 128:93188 Preparation and formulation of substituted piperidineamines as p antagonists for treating social phobia. Struck, Michael; Vassout, Annick; Katz, Richard; Bennett, Deborah; Kramer, Lynn; Hauser, Kathleen (Novartis A.-G., Switz.; Struck, Michael; Vassout, Annick; Katz, Richard; Bennett, Deborah; Kramer, Lynn; Hauser, Kathleen). PCT Int. Appl. WO 9745119 A1 19971204, 69 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-EP2481 19970515. PRIORITY: US 1996-18336 19960524.

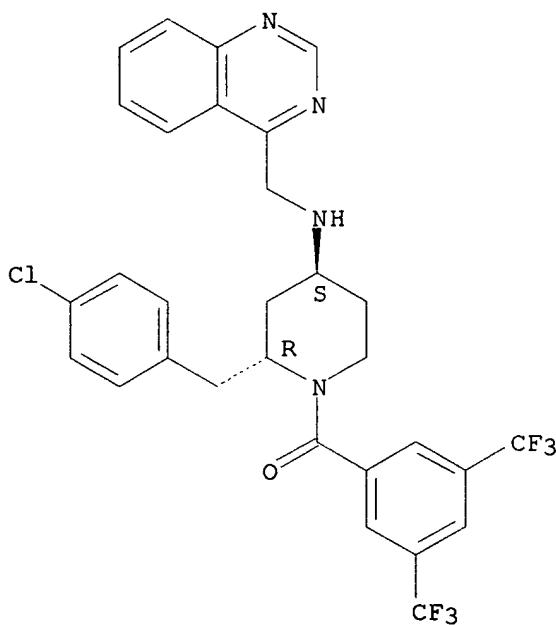
GI



AB The invention relates to the use of substituted piperidineamines I or of a pharmaceutically utilizable salt thereof, in which R1 is an unsubstituted or substituted aralkyl, aryloxyalkyl, heteroaralkyl, aroyl, heteroaroyl, cycloalkylcarbonyl, aralkanoyl, heteroarylalkanoyl, aralkoxycarbonyl or arylcarbamoyl radical or the acyl radical of an .alpha.-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl; R2 is cycloalkyl' or an unsubstituted or substituted aryl or heteroaryl radical; R3 is hydrogen, alkyl, carbamoyl or an alkanoyl or alkenoyl radical which is unsubstituted or substituted by carboxyl or esterified or amidated carboxyl; R4 is an unsubstituted or substituted aryl or unhydrogenated or partially hydrogenated heteroaryl radical; X1 is methylene, ethylene, a direct linkage, a carbonyl group which may be ketalized, or an unetherified or etherified hydroxymethylene group; X2 is alkylene, carbonyl or a direct linkage; and X3 is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or an alkylene radical which is unsubstituted or substituted by Ph, hydroxymethyl, carboxyl which may be esterified or amidated, or by hydroxyl in a position higher than .alpha.; for producing pharmaceutical products for the treatment of social phobia. Thus, the prepn. and formulation of (2R,2S)-2-benzyl-1-(2-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine as p antagonists for treating social phobia, are reported.

L7 ANSWER 35 OF 42 REGISTRY COPYRIGHT 2003 ACS  
 RN 200641-60-7 REGISTRY  
 CN 4-Piperidinamine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[4-chlorophenyl)methyl]-N-(4-quinazolinylmethyl)-, (2R-trans)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C30 H25 Cl F6 N4 O  
 SR CA  
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.

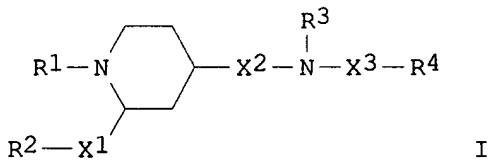


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REFERENCE 1: 128:93188 Preparation and formulation of substituted piperidineamines as p antagonists for treating social phobia. Struck, Michael; Vassout, Annick; Katz, Richard; Bennett, Deborah; Kramer, Lynn; Hauser, Kathleen (Novartis A.-G., Switz.; Struck, Michael; Vassout, Annick; Katz, Richard; Bennett, Deborah; Kramer, Lynn; Hauser, Kathleen). PCT Int. Appl. WO 9745119 A1 19971204, 69 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-EP2481 19970515. PRIORITY: US 1996-18336 19960524.

GI



AB The invention relates to the use of substituted piperidineamines I or of a pharmaceutically utilizable salt thereof, in which R1 is an unsubstituted or substituted aralkyl, aryloxyalkyl, heteroaralkyl, aroyl, heteroaroyl,

cycloalkylcarbonyl, aralkanoyl, heteroarylalkanoyl, aralkoxycarbonyl or arylcarbamoyl radical or the acyl radical of an .alpha.-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl; R2 is cycloalkyl or an unsubstituted or substituted aryl or heteroaryl radical; R3 is hydrogen, alkyl, carbamoyl or an alkanoyl or alkenoyl radical which is unsubstituted or substituted by carboxyl or esterified or amidated carboxyl; R4 is an unsubstituted or substituted aryl or unhydrogenated or partially hydrogenated heteroaryl radical; X1 is methylene, ethylene, a direct linkage, a carbonyl group which may be ketalized, or an unetherified or etherified hydroxymethylene group; X2 is alkylene, carbonyl or a direct linkage; and X3 is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or an alkylene radical which is unsubstituted or substituted by Ph, hydroxymethyl, carboxyl which may be esterified or amidated, or by hydroxyl in a position higher than .alpha.; for producing pharmaceutical products for the treatment of social phobia. Thus, the prepn. and formulation of (2R,2S)-2-benzyl-1-(2-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine as p antagonists for treating social phobia, are reported.

L7 ANSWER 36 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 145816-01-9 REGISTRY

CN Quinazoline, 4-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Quinazoline, 4-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-, (Z)-2-butenedioate (1:1)

FS STEREOSEARCH

MF C22 H25 N3 . C4 H4 O4

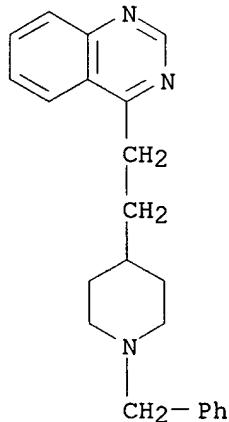
SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

CM 1

CRN 145508-81-2

CMF C22 H25 N3

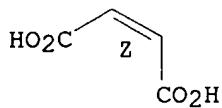


CM 2

CRN 110-16-7

CMF C4 H4 O4

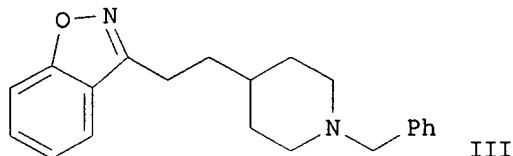
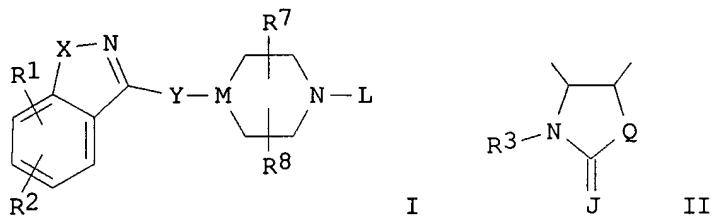
Double bond geometry as shown.



4 REFERENCES IN FILE CA (1962 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 129:4661 Preparation of benzisoxazoles and benzisothiazoles as cholinesterase inhibitors. Villalobos, Anabella; Nagel, Arthur A.; Chen, Yuhpyng L. (Pfizer Inc., USA). U.S. US 5750542 A 19980512, 33 pp. (English). CODEN: USXXAM. APPLICATION: US 1993-127847 19930928.

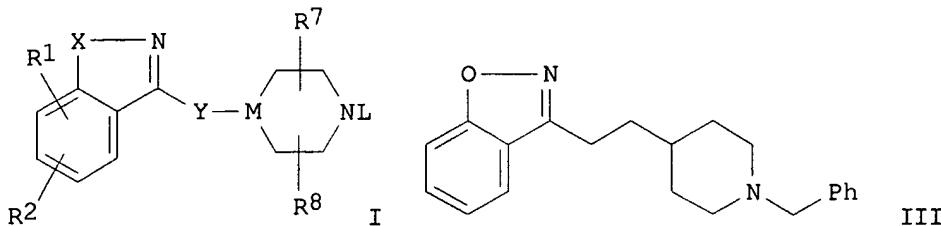
GI



AB The title compds. [I; R1 and R2 are attached to adjacent carbon atoms and form, together with the carbon atoms to which they are attached, a group II (wherein J = O, S, NR4; R4 = H, C1-4 alkyl; R3 = H, C1-6 alkyl; Q = (CH2)t; T = 1); R1, R2 = H, OH, PhO, etc.; X = O, S; Y = (CH2)m, O(CH2)m, CH:CH(CH2)n, NR4(CH2)m (n = 0-3; m = 1-2); M = CH; L = (un)substituted Ph, phenyl-(C1-6 alkyl), cinnamyl, pyridylmethyl; R7, R8 = H, C1-6 alkyl, C1-6 alkoxy, etc.] and their salts, useful in enhancing memory in patients suffering from dementia and Alzheimer's disease, were prep'd. Thus, 5-step synthesis of the title compd. III.maleate, starting from Et isonipeotate, was described. Compds. I are effective at 0.01-1 mg/day for the av. adult human.

REFERENCE 2: 125:195639 Methods of using piperidyl-benzisoxazole and benzisothiazole derivatives as cholinesterase inhibitors. Villalobos, Anabella; Nagel, Arthur A.; Chen, Yuhpyng L. (Pfizer Inc., USA). U.S. US 5538984 A 19960723, 33 pp., Division of U.S. Ser. No. 127,847. (English). CODEN: USXXAM. APPLICATION: US 1995-445814 19950522. PRIORITY: US 1993-127847 19930928.

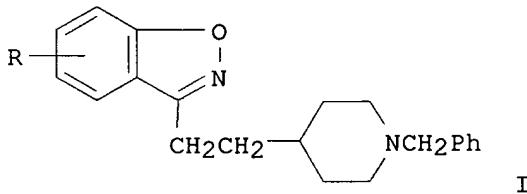
GI



AB The invention relates to compds. I [R1, R2 = H, OH, alkoxy, (un)substituted PhCH<sub>2</sub>O, PhO, Ph, or PhCH<sub>2</sub>, halo, NO<sub>2</sub>, nitro, cyano, (un)substituted amino, etc.; or R1R2 may form certain heterocyclic rings; X = O, S, CH:CH, CH:N, N:CH, N:N, NR<sub>4</sub>; R<sub>4</sub> = H, alkyl; Y = (CH<sub>2</sub>)<sub>m</sub>, CH:CH(CH<sub>2</sub>)<sub>n</sub>, NR<sub>4</sub>(CH<sub>2</sub>)<sub>m</sub>, or O(CH<sub>2</sub>)<sub>m</sub>; n = 0-3 and m = 1-3; M = CH or N; L = (un)substituted Ph, phenylalkyl, cinnamyl, pyridylmethyl, or sidechains contg. other 5-membered arom. heterocycles; R<sub>7</sub>, R<sub>8</sub> = H, alkyl, alkoxy carbonyl, alkyl carbonyl, alkoxy, with the proviso that alkoxy is not attached to a C which is adjacent to N]. I are cholinesterase inhibitors, useful for enhancing memory in patients suffering from dementia and Alzheimer's disease (no data). Examples include 36 syntheses of I plus various salts and intermediates. For instance, Et isonipeptate underwent N-BOC protection (94%), redn. of the ester with LiAlH<sub>4</sub> to give the (hydroxymethyl) analog (93%), and conversion of this to the (iodomethyl) analog, i.e. 4-(iodomethyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester (II) (92%). Then, 3-methyl-1,2-benzisoxazole was  $\alpha$ -lithiated with LiN(Pr-iso)<sub>2</sub> and coupled with II (42%), followed by deprotection and N-benzylation (73%) to give title compd. III, which was converted to its maleate (87%).

REFERENCE 3: 121:179520 Novel Benzisoxazole Derivatives as Potent and Selective Inhibitors of Acetylcholinesterase. Villalobos, Anabella; Blake, James F.; Biggers, C. Kelly; Butler, Todd W.; Chapin, Douglas S.; Chen, Yuhpyng L.; Ives, Jeffrey L.; Jones, Shawn B.; Liston, Dane R.; Nagel, Arthur A.; Nason, Deane M.; Nielsen, Jann A.; Shalaby, Ismail A.; White, W. Frost (Department of Medicinal Chemistry, Pfizer Inc., Groton, CT, 06340, USA). Journal of Medicinal Chemistry, 37(17), 2721-34 (English) 1994. CODEN: JMCMAR. ISSN: 0022-2623.

GI

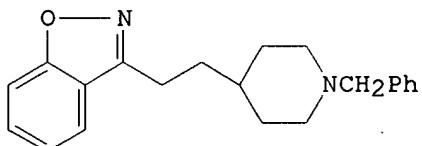


AB A series of N-benzylpiperidine benzisoxazoles I [R = H, 5-Me, 5,6-Me<sub>2</sub>, 5-OMe, 6-OMe, 7-OMe, 6-NHAc, 6-NHSO<sub>2</sub>Ph, 6-morpholino, 6-NH<sub>2</sub>, 6-OH, 6-Br, 6-CN, 6-CONH<sub>2</sub>] and some related compds. has been developed as potent and selective inhibitors of the enzyme acetylcholinesterase (AChE). The benzisoxazole heterocycle was found to be an appropriate bioisosteric replacement for the benzoyl functionality present in the N-benzylpiperidine class of inhibitors. The title compds. were

synthesized by alkylating 3-methyl-1,2-benzisoxazoles with an iodo piperidine deriv. as the key step. I displayed potent inhibition of AChE in vitro with IC<sub>50</sub>'s = 0.8-14 nM. Particularly interesting were I [R = 6-NHAc, morpholino] with IC<sub>50</sub> = 3 nM and 0.8 nM, resp., which displayed outstanding selectivity for acetyl- over butyrylcholinesterase, in excess of 3 orders of magnitude. I [R = NHAc] also displayed a favorable profile in vivo. This analog showed a dose-dependent elevation of total acetylcholine in mouse forebrain after oral administration with an ED<sub>50</sub> = 2.4 mg/kg. In addn., I [R = NHAc] was able to reverse amnesia in a mouse passive avoidance model at doses of 3.2 and 5.6 mg/kg with an av. reversal of 89.7%. Mol. dynamics simulations were used to study the possible binding modes of I to AChE from *Torpedo californica*. Key structural insights were obtained regarding the potency of this class of inhibitors. Specifically, Asp-72, Trp-84, Trp-279, Phe-288, and Phe-330 are implicated in the binding of these inhibitors. I may be suitable compds. for the palliative treatment of Alzheimer's Disease.

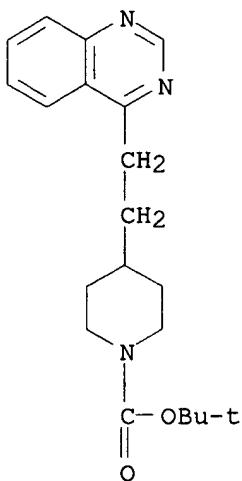
REFERENCE 4: 118:80924 Heterocyclic-cyclic amine derivatives, [(1-benzyl-4-piperidinyl)alkyl]benzisoxazoles and heteroaryl analogs, a method for their preparation and their use as cholinesterase inhibitors. Villalobos, Anabella; Nagel, Arthur Adam; Chen, Yuhpyng Liang (Pfizer Inc., USA). PCT Int. Appl. WO 9217475 A1 19921015, 120 pp. DESIGNATED STATES: W: AU, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US1605 19920309. PRIORITY: US 1991-676918 19910328.

GI



AB Heterocyclic amine derivs., such as [(1-benzyl-4-piperidinyl)alkyl]benzisoxazoles, -isoquinolines, -benzisothiazoles, -quinazolines and analogs and derivs. thereof are claimed. These compds. are useful as memory enhancers and for the treatment or prevention of Alzheimer's disease; these compds. are cholinesterase inhibitors (no data). Thus 3-[2-[(1-benzyl)-4-piperidinyl]ethyl]-1,2-benzisoxazole (I) was prep'd. from Et isonicotinate and 3-methyl-1,2-benzisoxazole in a multistep synthesis. The biol. activity of I was not tested.

L7 ANSWER 37 OF 42 REGISTRY COPYRIGHT 2003 ACS  
 RN 145509-15-5 REGISTRY  
 CN 1-Piperidinecarboxylic acid, 4-[2-(4-quinazolinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)  
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 LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

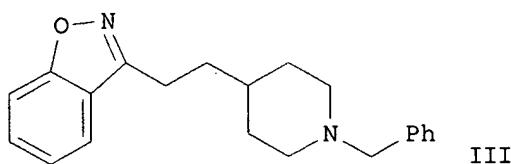
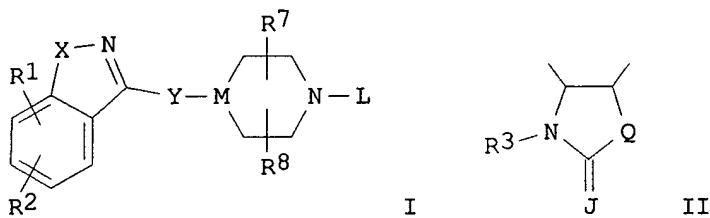


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4 REFERENCES IN FILE CA (1962 TO DATE)  
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GI

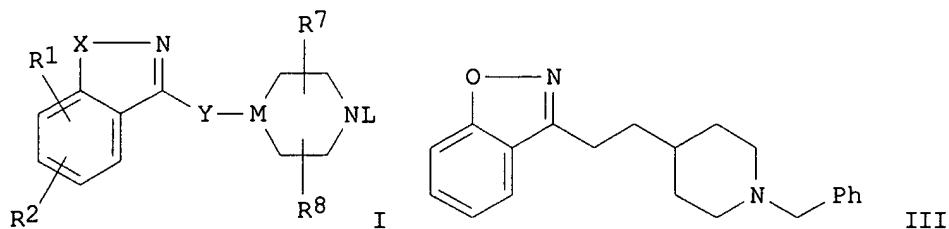


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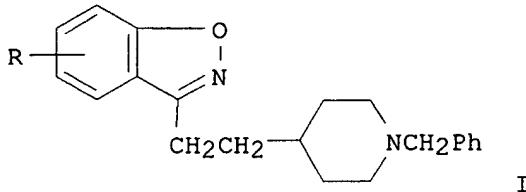
GI



AB The invention relates to compds. I [R1, R2 = H, OH, alkoxy, (un)substituted PhCH2O, PhO, Ph, or PhCH2, halo, NO2, nitro, cyano, (un)substituted amino, etc.; or R1R2 may form certain heterocyclic rings; X = O, S, CH:CH, CH:N, N:CH, N:N, NR4; R4 = H, alkyl; Y = (CH2)m, CH:CH(CH2)n, NR4(CH2)m, or O(CH2)m; n = 0-3 and m = 1-3; M = CH or N; L = (un)substituted Ph, phenylalkyl, cinnamyl, pyridylmethyl, or sidechains contg. other 5-membered arom. heterocycles; R7, R8 = H, alkyl, alkoxy carbonyl, alkyl carbonyl, alkoxy, with the proviso that alkoxy is not attached to a C which is adjacent to N]. I are cholinesterase inhibitors, useful for enhancing memory in patients suffering from dementia and Alzheimer's disease (no data). Examples include 36 syntheses of I plus various salts and intermediates. For instance, Et isonipecotate underwent N-BOC protection (94%), redn. of the ester with LiAlH4 to give the (hydroxymethyl) analog (93%), and conversion of this to the (iodomethyl) analog, i.e. 4-(iodomethyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester (II) (92%). Then, 3-methyl-1,2-benzisoxazole was  $\alpha$ -lithiated with LiN(Pr-iso)2 and coupled with II (42%), followed by deprotection and N-benzylation (73%) to give title compd. III, which was converted to its maleate (87%).

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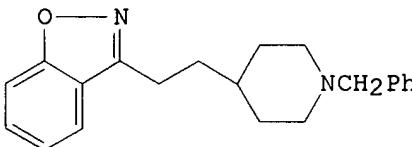
GI



AB A series of N-benzylpiperidine benzisoxazoles I [R = H, 5-Me, 5,6-Me<sub>2</sub>, 5-OMe, 6-OMe, 7-OMe, 6-NHAc, 6-NHSO<sub>2</sub>Ph, 6-morpholino, 6-NH<sub>2</sub>, 6-OH, 6-Br, 6-CN, 6-CONH<sub>2</sub>] and some related compds. has been developed as potent and selective inhibitors of the enzyme acetylcholinesterase (AChE). The benzisoxazole heterocycle was found to be an appropriate bioisosteric replacement for the benzoyl functionality present in the N-benzylpiperidine class of inhibitors. The title compds. were synthesized by alkylating 3-methyl-1,2-benzisoxazoles with an iodo piperidine deriv. as the key step. I displayed potent inhibition of AChE in vitro with IC<sub>50</sub>'s = 0.8-14 nM. Particularly interesting were I [R = 6-NHAc, morpholino] with IC<sub>50</sub> = 3 nM and 0.8 nM, resp., which displayed outstanding selectivity for acetyl- over butyrylcholinesterase, in excess of 3 orders of magnitude. I [R = NHAc] also displayed a favorable profile in vivo. This analog showed a dose-dependent elevation of total acetylcholine in mouse forebrain after oral administration with an ED<sub>50</sub> = 2.4 mg/kg. In addn., I [R = NHAc] was able to reverse amnesia in a mouse passive avoidance model at doses of 3.2 and 5.6 mg/kg with an av. reversal of 89.7%. Mol. dynamics simulations were used to study the possible binding modes of I to AChE from *Torpedo californica*. Key structural insights were obtained regarding the potency of this class of inhibitors. Specifically, Asp-72, Trp-84, Trp-279, Phe-288, and Phe-330 are implicated in the binding of these inhibitors. I may be suitable compds. for the palliative treatment of Alzheimer's Disease.

REFERENCE 4: 118:80924 Heterocyclic-cyclic amine derivatives, [(1-benzyl-4-piperidinyl)alkyl]benzisoxazoles and heteroaryl analogs, a method for their preparation and their use as cholinesterase inhibitors. Villalobos, Anabella; Nagel, Arthur Adam; Chen, Yuhpyng Liang (Pfizer Inc., USA). PCT Int. Appl. WO 9217475 A1 19921015, 120 pp. DESIGNATED STATES: W: AU, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US1605 19920309. PRIORITY: US 1991-676918 19910328.

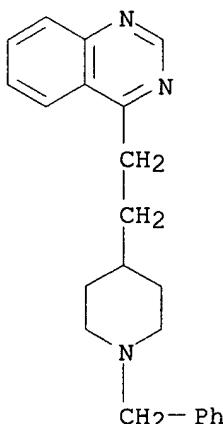
GI



AB Heterocyclic amine derivs., such as [(1-benzyl-4-piperidinyl)alkyl]benzisoxazoles, -isoquinolines, -benzisothiazoles, -quinazolines and analogs and derivs. thereof are claimed. These compds. are useful as memory enhancers and for the treatment or prevention of Alzheimer's disease; these compds. are cholinesterase inhibitors (no

data). Thus 3-[2-[(1-benzyl)-4-piperidinyl]ethyl]-1,2-benzisoxazole (I) was prep'd. from Et isonipecotate and 3-methyl-1,2-benzisoxazole in a multistep synthesis. The biol. activity of I was not tested.

L7 ANSWER 38 OF 42 REGISTRY COPYRIGHT 2003 ACS  
RN 145508-81-2 REGISTRY  
CN Quinazoline, 4-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H25 N3  
CI COM  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8 REFERENCES IN FILE CA (1962 TO DATE)  
8 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:251415 Electronic-topological investigation of the structure - acetylcholinesterase inhibitor activity relationship in the series of N-benzylpiperidine derivatives. Dimoglo, A. S.; Shvets, N. M.; Tetko, I. V.; Livingstone, D. J. (Institute of Chemistry, Academy of Sciences, Chisinau, MD-2028, Moldova). Quantitative Structure-Activity Relationships, 20(1), 31-45 (English) 2001. CODEN: QSARDI. ISSN: 0931-8771. Publisher: Wiley-VCH Verlag GmbH.

AB Structure-acetylcholinesterase (AChE) inhibitor activity relationship studies have been performed for three series of N-benzylpiperidine derivs. using the Electronic-Topol. Method (ETM) which is a structural approach designed for the investigation of structure-property relationships. Biol. activities of the compds. belonging to three different series have been measured on mouse, human and *Torpedo californica* AChE. Mol. fragments that are only specific for active compds. (activity features) were found for each of these series. In a similar way, breaks of activity (i.e., mol. fragments that are typical of inactive compds. and cannot be a part of an active compd.) were calcd. by applying the ETM. Requirements necessary for a compd. to be active are formulated; they are the result of a detailed anal. of all compds. under study. The anal. shows that any violation of these requirements for a mol. decreases considerably or even provokes a complete loss of its activity. A comparative study of the activity features found relative to three different AChE has also been

performed.

REFERENCE 2: 132:329435 Validation of protein-based alignment in 3D quantitative structure-activity relationships with CoMFA models. Golbraikh, Alexander; Bernard, Philippe; Chretien, Jacques R. (Laboratory of Chemometrics and Bioinformatics, University of Orleans, Orleans, 45067, Fr.). European Journal of Medicinal Chemistry, 35(1), 123-136 (English) 2000. CODEN: EJMCA5. ISSN: 0223-5234. Publisher: Editions Scientifiques et Medicales Elsevier.

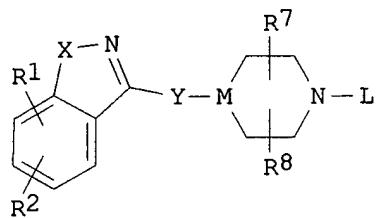
AB The predictive capabilities of protein-based alignment (PBA) and structure-based alignment (SBA) comparative mol. field anal. (CoMFA) models have been compared. 3D quant. structure-activity relationship (3D QSAR) models have been derived for a series of N-benzylpiperidine derivs. which are potent acetylcholinesterase (AChE) inhibitors interesting for Alzheimer's disease. To establish a comparison with the classical SBA procedure, different assay models were derived by superposing ligand conformers that are docked to the AChE active site and by using the most active compd. as the ref. one. A Kohonen self organizing map (SOM) was applied to analyze the mol. diversity of the test set relative to that of the training set, in order to explain the influence of mol. diversity on the predictive power of the considered models. SBA 3D QSAR models have to be used to predict the inhibitory activity only for compds. belonging to subgroups included in the training set. The PBA 3D QSAR models appeared to have a higher predictability, even for compds. with a mol. diversity greater than that of the training set. This results from the fact that the protein helps to automatically select the active conformation which is fitting the 3D QSAR model.

REFERENCE 3: 131:252093 Automated docking of 82 N-benzylpiperidine derivatives to mouse acetylcholinesterase and comparative molecular field analysis with "natural" alignment. Bernard, Philippe; Kireev, Dmitri B.; Chretien, Jacques R.; Fortier, Pierre-Louis; Coppet, Lucien (Laboratoire de Chimie et de Physique, Universite d'Orleans, Orleans, F-45067, Fr.). Journal of Computer-Aided Molecular Design, 13(4), 355-371 (English) 1999. CODEN: JCADEQ. ISSN: 0920-654X. Publisher: Kluwer Academic Publishers.

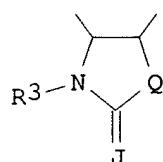
AB Automated docking and three-dimensional Quant. Structure-Activity Relationship studies (3D QSAR) were performed for a series of 82 reversible, competitive and selective acetylcholinesterase (AChE) inhibitors. The suggested automated docking technique, making use of constraints taken from exptl. crystallog. data, allowed to dock all the 82 substituted N-benzylpiperidines to the crystal structure of mouse AChE, because of short computational times. A 3D QSAR model was then established using the CoMFA method. In contrast to conventional CoMFA studies, the compds. were not fitted to a ref. mol. but taken in their "natural" alignment obtained by the docking study. The established and validated CoMFA model was then applied to another series of 29 N-benzylpiperidine derivs. whose AChE inhibitory activity data were measured under different exptl. conditions. A good correlation between predicted and exptl. activity data shows that the model can be extended to AChE inhibitory activity data measured on another acetylcholinesterase and/or at different incubation times and pH level.

REFERENCE 4: 129:4661 Preparation of benzisoxazoles and benzisothiazoles as cholinesterase inhibitors. Villalobos, Anabella; Nagel, Arthur A.; Chen, Yuhpyng L. (Pfizer Inc., USA). U.S. US 5750542 A 19980512, 33 pp. (English). CODEN: USXXAM. APPLICATION: US 1993-127847 19930928.

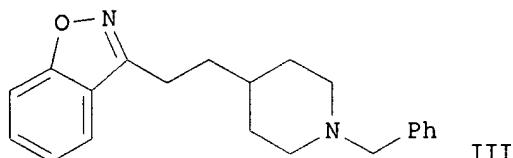
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I



II

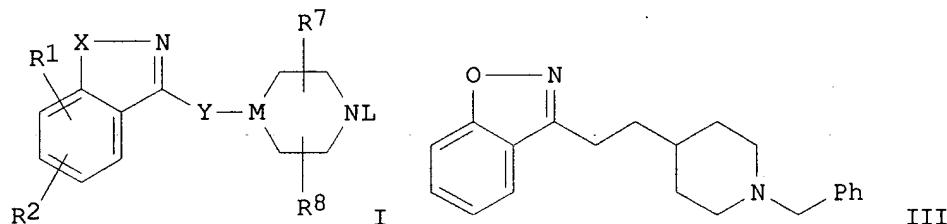


III

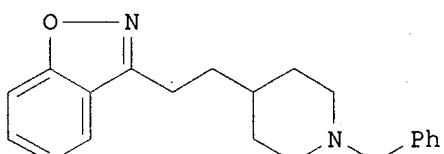
AB The title compds. [I; R1 and R2 are attached to adjacent carbon atoms and form, together with the carbon atoms to which they are attached, a group II (wherein J = O, S, NR4; R4 = H, C1-4 alkyl; R3 = H, C1-6 alkyl; Q = (CH2)t; T = 1); R1, R2 = H, OH, PhO, etc.; X = O, S; Y = (CH2)m, O(CH2)m, CH:CH(CH2)n, NR4(CH2)m (n = 0-3; m = 1-2); M = CH; L = (un)substituted Ph, phenyl-(C1-6 alkyl), cinnamyl, pyridylmethyl; R7, R8 = H, C1-6 alkyl, C1-6 alkoxy, etc.] and their salts, useful in enhancing memory in patients suffering from dementia and Alzheimer's disease, were prep'd. Thus, 5-step synthesis of the title compd. III.maleate, starting from Et isonipecotate, was described. Compds. I are effective at 0.01-1 mg/day for the av. adult human.

REFERENCE 5: 125:195639 Methods of using piperidyl-benzisoxazole and benzisothiazole derivatives as cholinesterase inhibitors. Villalobos, Anabella; Nagel, Arthur A.; Chen, Yuhpyng L. (Pfizer Inc., USA). U.S. US 5538984 A 19960723, 33 pp., Division of U.S. Ser. No. 127,847. (English). CODEN: USXXAM. APPLICATION: US 1995-445814 19950522. PRIORITY: US 1993-127847 19930928.

GI



I



III

AB The invention relates to compds. I [R1, R2 = H, OH, alkoxy, (un)substituted PhCH2O, PhO, Ph, or PhCH2, halo, NO2, nitro, cyano, (un)substituted amino, etc.; or R1R2 may form certain heterocyclic rings; X = O, S, CH:CH, CH:N, N:CH, N:N, NR4; R4 = H, alkyl; Y = (CH2)m, CH:CH(CH2)n, NR4(CH2)m, or O(CH2)m; n = 0-3 and m = 1-3; M = CH or N; L = (un)substituted Ph, phenylalkyl, cinnamyl, pyridylmethyl, or sidechains contg. other 5-membered arom. heterocycles; R7, R8 = H, alkyl,

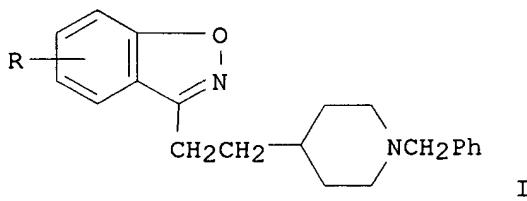
alkoxycarbonyl, alkylcarbonyl, alkoxy, with the proviso that alkoxy is not attached to a C which is adjacent to N]. I are cholinesterase inhibitors, useful for enhancing memory in patients suffering from dementia and Alzheimer's disease (no data). Examples include 36 syntheses of I plus various salts and intermediates. For instance, Et isonipeptate underwent N-BOC protection (94%), redn. of the ester with LiAlH<sub>4</sub> to give the (hydroxymethyl) analog (93%), and conversion of this to the (iodomethyl) analog, i.e. 4-(iodomethyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester (II) (92%). Then, 3-methyl-1,2-benzisoxazole was  $\alpha$ -lithiated with LiN(Pr-iso)<sub>2</sub> and coupled with II (42%), followed by deprotection and N-benzylation (73%) to give title compd. III, which was converted to its maleate (87%).

REFERENCE 6: 124:105610 A Comparative Molecular Field Analysis Study of N-Benzylpiperidines as Acetylcholinesterase Inhibitors. Tong, Weida; Collantes, Elizabeth R.; Chen, Yu; Welsh, William J. (Department of Chemistry, University of Missouri, St. Louis, MO, 63121, USA). Journal of Medicinal Chemistry, 39(2), 380-7 (English) 1996. CODEN: JMCMAR. ISSN: 0022-2623. Publisher: American Chemical Society.

AB A series of 1-benzyl-4-[2-(N-benzoylamino)ethyl]piperidine derivs. and of N-benzylpiperidine benzisoxazoles have been investigated using the comparative mol. field anal. (CoMFA) approach. These compds. have been found to inhibit the metabolic breakdown of the neurotransmitter acetylcholine (ACh) by the enzyme acetylcholinesterase (AChE) and hence alleviate memory deficits in patients with Alzheimer's disease by potentiating cholinergic transmission. Development of the CoMFA model considered two sep. alignments: (i) alignment I which emphasized the electrostatic fitting of the subject compds. and (ii) alignment II which emphasized their steric fitting. In addn., the inhibitor compds. were considered both as neutral species and as N-piperidine-protonated species. The resulting 3D-QSAR indicates a strong correlation between the inhibitory activity of these N-benzylpiperidines and the steric and electronic factors which modulate their biochem. activity. A CoMFA model with considerable predictive ability was obtained.

REFERENCE 7: 121:179520 Novel Benzisoxazole Derivatives as Potent and Selective Inhibitors of Acetylcholinesterase. Villalobos, Anabella; Blake, James F.; Biggers, C. Kelly; Butler, Todd W.; Chapin, Douglas S.; Chen, Yuhpyng L.; Ives, Jeffrey L.; Jones, Shawn B.; Liston, Dane R.; Nagel, Arthur A.; Nason, Deane M.; Nielsen, Jann A.; Shalaby, Ismail A.; White, W. Frost (Department of Medicinal Chemistry, Pfizer Inc., Groton, CT, 06340, USA). Journal of Medicinal Chemistry, 37(17), 2721-34 (English) 1994. CODEN: JMCMAR. ISSN: 0022-2623.

GI

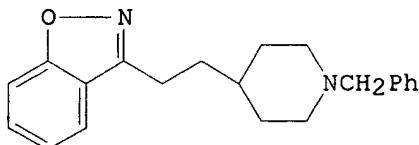


AB A series of N-benzylpiperidine benzisoxazoles I [R = H, 5-Me, 5,6-Me<sub>2</sub>, 5-OMe, 6-OMe, 7-OMe, 6-NHAc, 6-NHSO<sub>2</sub>Ph, 6-morpholino, 6-NH<sub>2</sub>, 6-OH, 6-Br, 6-CN, 6-CONH<sub>2</sub>] and some related compds. has been developed as potent and selective inhibitors of the enzyme acetylcholinesterase (AChE). The

benzisoxazole heterocycle was found to be an appropriate bioisosteric replacement for the benzoyl functionality present in the N-benzylpiperidine class of inhibitors. The title compds. were synthesized by alkylating 3-methyl-1,2-benzisoxazoles with an iodo piperidine deriv. as the key step. I displayed potent inhibition of AChE in vitro with IC<sub>50</sub>'s = 0.8-14 nM. Particularly interesting were I [R = 6-NHAc, morpholino] with IC<sub>50</sub> = 3 nM and 0.8 nM, resp., which displayed outstanding selectivity for acetyl- over butyrylcholinesterase, in excess of 3 orders of magnitude. I [R = NHAc] also displayed a favorable profile in vivo. This analog showed a dose-dependent elevation of total acetylcholine in mouse forebrain after oral administration with an ED<sub>50</sub> = 2.4 mg/kg. In addn., I [R = NHAc] was able to reverse amnesia in a mouse passive avoidance model at doses of 3.2 and 5.6 mg/kg with an av. reversal of 89.7%. Mol. dynamics simulations were used to study the possible binding modes of I to AChE from *Torpedo californica*. Key structural insights were obtained regarding the potency of this class of inhibitors. Specifically, Asp-72, Trp-84, Trp-279, Phe-288, and Phe-330 are implicated in the binding of these inhibitors. I may be suitable compds. for the palliative treatment of Alzheimer's Disease.

REFERENCE 8: 118:80924 Heterocyclic-cyclic amine derivatives, [(1-benzyl-4-piperidinyl)alkyl]benzisoxazoles and heteroaryl analogs, a method for their preparation and their use as cholinesterase inhibitors. Villalobos, Anabella; Nagel, Arthur Adam; Chen, Yuhpyng Liang (Pfizer Inc., USA). PCT Int. Appl. WO 9217475 A1 19921015, 120 pp. DESIGNATED STATES: W: AU, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US1605 19920309. PRIORITY: US 1991-676918 19910328.

GI



AB Heterocyclic amine derivs., such as [(1-benzyl-4-piperidinyl)alkyl]benzisoxazoles, -isoquinolines, -benzisothiazoles, -quinazolines and analogs and derivs. thereof are claimed. These compds. are useful as memory enhancers and for the treatment or prevention of Alzheimer's disease; these compds. are cholinesterase inhibitors (no data). Thus 3-[2-[(1-benzyl)-4-piperidinyl]ethyl]-1,2-benzisoxazole (I) was prep'd. from Et isonicotinate and 3-methyl-1,2-benzisoxazole in a multistep synthesis. The biol. activity of I was not tested.

L7 ANSWER 39 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 110441-94-6 REGISTRY

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FS STEREOSEARCH

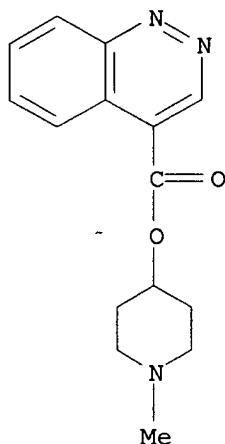
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SR CAOLD

LC STN Files: CAOLD

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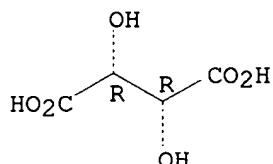
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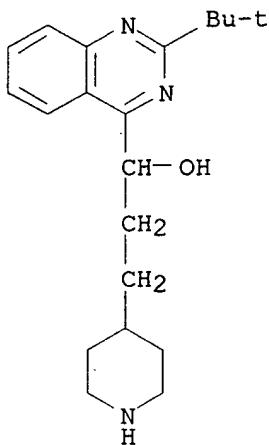
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Absolute stereochemistry.



1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L7 ANSWER 40 OF 42 REGISTRY COPYRIGHT 2003 ACS  
RN 101687-86-9 REGISTRY  
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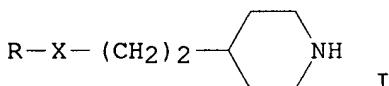
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
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REFERENCE 1: 104:161984 Piperidine derivatives and their therapeutic use.  
 Renault, Christian; Mestre, Michel (Rhone-Poulenc Sante, Fr.). Fr.  
 Demande FR 2560873 A1 19850913, 16 pp. (French). CODEN: FRXXBL.

APPLICATION: FR 1984-3670 19840309.

GI



AB A group of piperidine derivs. I (X = CO, CHO, CHNH2; R = 1-naphthyl, 2-naphthyl, 1-isoquinolinyl, 4-quinazolinyl) useful as antiarrhythmic agents are described. Thus, 1-(2-naphthyl)-3-(4-piperidyl)-1-propanone 2.5 was prep'd. by condensation of Et 2-naphthoate 5.5 with Et 2-benzoyl-3-(4-piperidyl)propionate 7.0 g in the presence of KH. Nine compds. were tested against aconitine-induced arrhythmia in rats. The ED50 of the compds. ranged 0.3-4 mg/kg i.v. compared to 7.5 mg/kg i.v. for quinidine. All these compds. exhibited LD50 >15 mg/kg i.v. in male mice.

L7 ANSWER 41 OF 42 REGISTRY COPYRIGHT 2003 ACS

RN 101687-82-5 REGISTRY

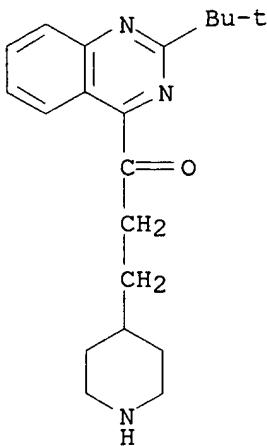
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FS 3D CONCORD

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SR CA

LC STN Files: CA, CAPLUS

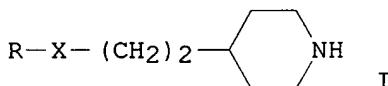


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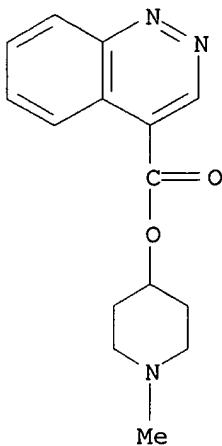
REFERENCE 1: 104:161984 Piperidine derivatives and their therapeutic use.  
 Renault, Christian; Mestre, Michel (Rhone-Poulenc Sante, Fr.). Fr.  
 Demande FR 2560873 A1 19850913, 16 pp. (French). CODEN: FRXXBL.  
 APPLICATION: FR 1984-3670 19840309.

GI



AB A group of piperidine derivs. I (X = CO, CHO, CHNH<sub>2</sub>; R = 1-naphthyl, 2-naphthyl, 1-isoquinolinyl, 4-quinazolinyl) useful as antiarrhythmic agents are described. Thus, 1-(2-naphthyl)-3-(4-piperidyl)-1-propanone 2.5 was prep'd. by condensation of Et 2-naphthoate 5.5 with Et 2-benzoyl-3-(4-piperidyl)propionate 7.0 g in the presence of KH. Nine compds. were tested against aconitine-induced arrhythmia in rats. The ED<sub>50</sub> of the compds. ranged 0.3-4 mg/kg i.v. compared to 7.5 mg/kg i.v. for quinidine. All these compds. exhibited LD<sub>50</sub> >15 mg/kg i.v. in male mice.

L7 ANSWER 42 OF 42 REGISTRY COPYRIGHT 2003 ACS  
 RN 100973-57-7 REGISTRY  
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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L8 ANSWER 1 OF 1 CAOLD COPYRIGHT 2003 ACS  
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Searched by: Mary Hale 308-4258 CM-1 1E01

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BIOSIS - The BIOSIS Previews(R)/RN File 1969-present

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L9 0 FILE MEDLINE  
L10 0 FILE BIOSIS  
L11 3 FILE CAPPLUS

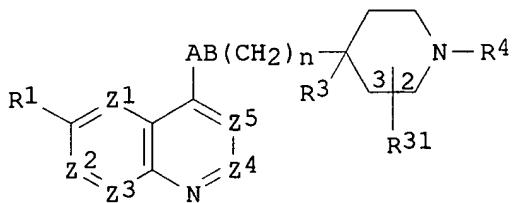
TOTAL FOR ALL FILES

L12 3 L7 AND (INFECT? OR BACTER? INFECT?)

=> d 1-3 cbib abs;s davies, d?/au;s henry, c?/au;s pearson, n?/au

L12 ANSWER 1 OF 3 CAPPLUS COPYRIGHT 2003 ACS

2003:97394 Document No. 138:153541 Preparation of N-(1,5-naphthyridin-4-yl)piperidine-4-carboxamide derivatives as antibacterial agents. Davies, David Thomas; Jones, Graham Elgin; Markwell, Roger Edward; Pearson, Neil David (Smithkline Beecham PLC, UK). PCT Int. Appl. WO 2003010138 A2 20030206, 97 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP8319 20020725. PRIORITY: GB



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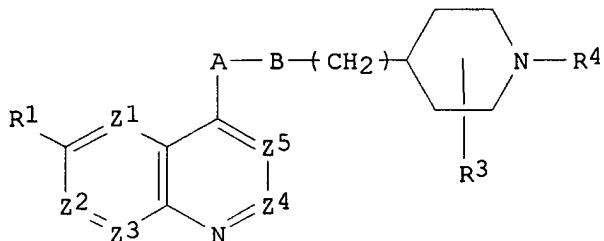
AB The title piperidine derivs. [I; one of Z1-Z5 is N, one is CR1a and the remainder are CH, or one or two of Z1-Z5 are independently CR1 a and the remainder are CH; R1, R1a = H, HO, C1-6 alkoxy optionally substituted by (un)substituted C1-6 alkoxy, amino, piperidyl, guanidino or amidino, C1-6 alkoxy-C1-6 alkyl, halo, C1-6 alkyl, C1-6 alkylthio, CF3, CF3O, etc.; R3 = CO2H, C1-6 alkoxycarbonyl, (un)substituted CONH2, cyano, tetrazolyl, (un)substituted 2-oxooxazolidinyl, 3-hydroxy-3-cyclobutene-1,2-dione-4-yl, 2,4-thiazolidinedione-5-yl, tetrazol-5-ylaminocarbonyl, (un)substituted 1,2,4-triazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl, (un)substituted C1-4 alkyl or ethenyl, halogen, C1-6 alkylthio, CF3, C1-6 alkoxycarbonyl, C1-6 alkylcarbonyl, C2-6 alkenyloxycarbonyl, C2-6 alkenylcarbonyl, (un)substituted OH or NH2, etc.; R31 is in the 2- or 3-position and is hydrogen or a group listed above for R3, provided that R31 in the 2-position is not optionally substituted hydroxy, amino, trifluoromethyl or halogen; R4 = CH2R51, U-V-R52 (wherein R51 = C4-8 alkyl, hydroxy-C4-8 alkyl, C1-4 alkoxy-C4-8 alkyl, etc.; U = CO, SO2, CH2 and V = (un)substituted CH2; or U = CH2 and V = CO, (un)substituted C(:NOH), SO2; R52 = (un)substituted bicyclic carbocyclic or heterocyclic ring); n = 0,1; AB = (un)substituted NHCO, CONH, COCH2, CH2CO, OCH2, CH2O, NHCH2, CH2NH, NHSO2, CH2 SO2, CH2CH2] and pharmaceutically acceptable derivs. thereof are prepd. These compds. are useful in methods of treatment of **bacterial infections** in mammals, particularly man. Thus, 0.10 g 4-(6-methoxy-[1,5]naphthyridin-4-ylcarbamoyl)-4-methylpiperidine and 0.095 g 2-(3-Oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl methanesulfonate were stirred with 138 mg K2CO3 in 2 mL DMF at room temp. for 3 days to give 4-methyl-1-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-6-yl)ethyl]piperidine-4-carboxylic acid (6-methoxy-[1,5]naphthyridin-4-yl)amide (II). II oxalate showed min. inhibitory concn. of .1 to req. 4 .mu.g/mL against *Staphylococcus aureus* Oxford, *S. aureus* WCUH29, *S. pneumoniae* 1629, *S. pneumoniae* N1387, *S. pneumoniae* ERY 2, *Enterococcus faecalis* I, *E. faecalis* 7, *Haemophilus influenzae* Q1, *H. influenzae* NEMC1, *Moraxella catarrhalis* 1502, and *Escherichia coli* 7623.

L12 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

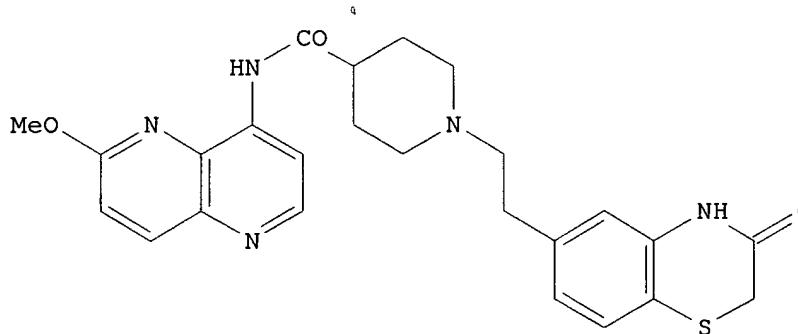
2002:927429 Document No. 138:14011 Preparation of bicyclic nitrogen-containing heterocyclic derivatives for use as antibacterials. Dartois, Catherine Genevieve Yvette; Markwell, Roger Edward; Madler, Guy Marguerite Marie Gerard; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2002096907 A1 20021205, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM,

CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP5709 20020524. PRIORITY: GB 2001-12836 20010525.

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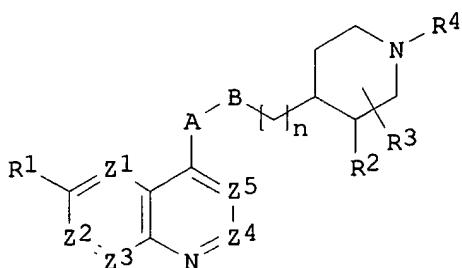


II

AB Piperidine derivs. and pharmaceutically acceptable derivs. [I; wherein one of Z1, Z2, Z3, Z4, Z5 = N, one is CR2 (wherein R2 = H, OH, (C1-C6)alkoxy, etc.) and the remainder are CH, or one of Z1, Z2, Z3, Z4, Z5 = CR2 and the remainder are CH; R3 = H, carboxy, (C1-C6)alkoxycarbonyl, aminocarbonyl, cyano, tetrazolyl, etc.; R4 = U-V-R5, wherein U-V = (CH2)2, CH2CH(OH), CH2CO, and R5 is a (substituted) bicyclic carbocyclic or heterocyclic ring system] were prepd. For example, II was prepd. by a multistep synthetic procedure. The prepd. compds. are useful in the treatment of **bacterial infections** in mammals, particularly man. For example, compd. II had MIC values  $1 \text{ to } 4 \text{ } \mu\text{g/mL}$  against *S. aureus* Oxford.

L12 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS

2000:260265 Document No. 132:293679 Preparation of naphthyridines and their azaisosteric analogues as antibacterials. Hatton, Ian Keith; Pearson, Neil David (Smithkline Beecham P.L.C., UK). PCT Int. Appl. WO 2000021948 A1 20000420, 38 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB3366 19991011. PRIORITY: GB 1998-22450 19981014.



AB The title compds. [I; one of Z<sub>1</sub>-Z<sub>5</sub> = N and the remainder are CH; R<sub>1</sub> = H, OH, alkoxy, etc.; either R<sub>2</sub> = H, and R<sub>3</sub> is in the 2- or 3-position and is H, alkyl, alkenyl, etc.; or R<sub>3</sub> is in the 3-position and R<sub>2</sub> and R<sub>3</sub> together are a divalent :CR<sub>6</sub>R<sub>7</sub> (wherein R<sub>6</sub> and R<sub>7</sub> = H, alkyl, alkenyl, etc.); R<sub>4</sub> = CH<sub>2</sub>R<sub>5</sub> (R<sub>5</sub> = alkyl, hydroxyalkyl, alkoxyalkyl, etc.); n = 0-2; A, B = NR<sub>8</sub>, O, SO<sub>x</sub>, etc.; x = 0-2; R<sub>8</sub> = H, CF<sub>3</sub>, alkyl, etc.] and their pharmaceutically acceptable derivs., useful in the treatment of **bacterial infections** in mammals, particularly in man, were prep'd. E.g., a multi-step synthesis of (3R,4S)-I [Z<sub>1</sub>-Z<sub>4</sub> = CH; Z<sub>5</sub> = N; R<sub>1</sub> = OMe; A = N(Me); B = CH<sub>2</sub>; n = 1; R<sub>2</sub> = CH:CH<sub>2</sub>; R<sub>3</sub> = H; R<sub>4</sub> = n-heptyl] which showed MIC of 0.5 .mu.g/mL against S. aureus Oxford, M. catarrhalis Ravasio and S. pneumoniae, was given.

L13 2161 FILE MEDLINE  
 L14 2459 FILE BIOSIS  
 L15 2731 FILE CAPLUS

TOTAL FOR ALL FILES  
 L16 7351 DAVIES, D?/AU

L17 487 FILE MEDLINE  
 L18 626 FILE BIOSIS  
 L19 825 FILE CAPLUS

TOTAL FOR ALL FILES  
 L20 1938 HENRY, C?/AU

L21 102 FILE MEDLINE  
 L22 110 FILE BIOSIS  
 L23 184 FILE CAPLUS

TOTAL FOR ALL FILES  
 L24 396 PEARSON, N?/AU

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 L26 0 FILE BIOSIS  
 L27 1 FILE CAPLUS

TOTAL FOR ALL FILES  
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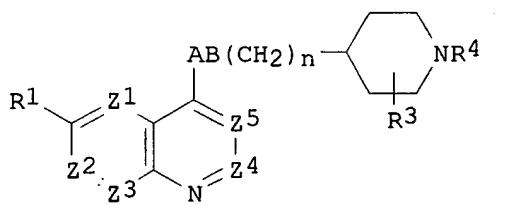
L28 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

2000:513687 Document No. 133:120244 Preparation of

piperidinylpropylquinolines and related compounds as protein tyrosine kinase inhibitors. **Davies, David Thomas; Henry, Caroline Joan; Pearson, Neil David** (Smithkline Beecham P.L.C., UK).

PCT Int. Appl. WO 2000043383 A1 20000727, 53 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP350 20000117. PRIORITY: GB 1999-1236 19990120; GB 1999-23936 19991008.

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AB A method of treatment of bacterial infection comprises administration of title compds. [I; 1 of Z1-Z5 = N, CR1a, the remainder = CH; R1 = OH, (substituted) alkoxy, alkoxyalkyl, halo, alkyl, alkylthio, CF3, NO2, acyl, acyloxy, N3, etc.; R1a = H, R1; R3 = CO2H, alkoxy carbonyl, aminocarbonyl, cyano, tetrazolyl, oxooxazolidinyl, substituted alkyl, ethenyl, etc.; R4 = CH2R5; R5 = alkyl, hydroxyalkyl, alkoxyalkyl, alkanoyloxyalkyl, (substituted) phenylalkyl, etc.; n = 0-2; AB = NHCONH, NHCO2, or A = NR11, O, S, SO, SO2, CR6R7, B = NR11, O, S, SO, SO2, CR8R9; R6-R9 = H, SH, alkylthio, halo, CF3, alkyl, etc.; R11 = H, CF3, alkyl, alkenyl, alkoxy carbonyl, alkyl carbonyl, etc.; with provisos]. Thus, 1-[3R,4R]-1-heptyl-3-(1-(R- or S)-hydroxy-2-cyanoethyl)-4-[3-(6-methoxyquinolin-4-yl)propyl]piperidine, prep'd. in several steps from quinine, showed min. inhibitory concns. of .1 to <1 .mu.g/mL against a range of gram-pos. and gram-neg. bacteria.

=> fil wpids

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION

FULL ESTIMATED COST

23.31	415.63
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION

CA SUBSCRIBER PRICE

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2 APR 2003

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Searched by: Mary Hale 308-4258 CM-1 1E01

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=> s davies, d?/in;s henry, c?/in;s pearson, n?/in  
L29 268 DAVIES, D?/IN

L30 114 HENRY, C?/IN

L31 51 PEARSON, N?/IN

=> s 129 and 130 and 131  
L32 1 L29 AND L30 AND L31

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L32 ANSWER 1 OF 1 WPIDS (C) 2003 THOMSON DERWENT  
AN 2000-532704 [48] WPIDS  
DNC C2000-158656  
TI Treatment of bacterial infections in mammals comprises administration of  
new and known piperidinylquinolines.  
DC B02  
IN DAVIES, D T; HENRY, C J; PEARSON, N D  
PA (SMIK) SMITHKLINE BEECHAM PLC  
CYC 91  
PI WO 2000043383 A1 20000727 (200048)\* EN 48p C07D401-06  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ TZ UG ZW  
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES  
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS  
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EP 1144404 A1 20011017 (200169) EN C07D401-06  
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RO SE SI  
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ADT WO 2000043383 A1 WO 2000-EP350 20000117; AU 2000024379 A AU 2000-24379  
20000117; EP 1144404 A1 EP 2000-902605 20000117, WO 2000-EP350 20000117;  
JP 2002535323 W JP 2000-594799 20000117, WO 2000-EP350 20000117  
FDT AU 2000024379 A Based on WO 200043383; EP 1144404 A1 Based on WO  
200043383; JP 2002535323 W Based on WO 200043383  
PRAI GB 1999-23936 19991008; GB 1999-1236 19990120  
IC ICM C07D401-06  
ICS A61K031-445; A61K031-4545; A61K031-47; A61K031-4709; A61P031-04;  
C07D401-12; C07D401-14; C07D405-14; C07D413-14; C07D471-04

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.64	422.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-27.40

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